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SYSTEM OF MEDICINE

BY MANY WRITERS

EDITED BY

THOMAS CLIFFORD ALLBUTT

M.A., M.D., LL.D., F.R.C.P., F.R.S., F.L.S., F.S.A.

REGIUS PROFESSOR OF PHYSIC IN THE UNIVERSITY OF CAMBRIDGE,
FELLOW OF GONVILLE AND CAIUS COLLEGE

VOLUME III

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PREFACE

THE delay in the issue of the Second Volume of the *System of Medicine* is due to the late appearance of the Report of the Commission on Vaccination. It seemed to the editor and publishers of this volume, and likewise to the authors of the three sections on Vaccination, that to publish these sections without the advantage of the labours of the Commissioners would be a worse evil than the delay of some months in issue.

As soon as the Report of the Commission was published the authors of the corresponding sections in this volume completed their several articles in as short a time as the difficulties of their task would permit. I owe them my sincere thanks for their loyal industry.

The issue meanwhile of the volume on Gynæcology testified, I trust, to the desire of the editor and of the publishers to fulfil their engagements with the public as punctually as circumstances permitted.

In respect of the future, I am glad to be able to say that the articles to appear in the third and fourth volumes are all in hand, and most of them are printed.

I have again to express my thanks to Dr. Rolleston for his valuable help in proof-reading and in many other ways; to Dr. Manson for reading the proofs of Professor Osler's article on Malaria; to Dr. Andrew Davidson for the same kind service for Dr. Lafleur, and to Mr. Shipley of Christ's College for final revision of some details of zoology.

The attention of the reader is directed to the appendixes on the Serum Diagnosis of Typhoid Fever, by Dr. Delépine; on the Serum cure of Plague, by Dr. Payne; and on the Bacteriology of Yellow Fever, by Dr. Davidson.

T. C. A.

CAMBRIDGE, 1897.

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LIST OF AUTHORS

Abraham, Phineas S., M.D., B.Sc., F.R.C.S.I., Assistant Surgeon to the Hospital for Skin Diseases, Blackfriars; Surgeon for Diseases of the Skin at the Westminster Hospital; Editor of *Journal of Leprosy Investigation Committee.*

Acland, Theodore Dyke, M.D., F.R.C.P., Physician to St. Thomas's Hospital and to the Brompton Hospital for Diseases of the Chest; one of the Medical Officers to the Royal Commission on Vaccination, 1889-96.

Allbutt, Thomas Clifford, M.D., LL.D., F.R.C.P., F.R.S., Regius Professor of Physic in the University of Cambridge, Fellow of Gonville and Caius College, Consulting Physician to the Leeds General Infirmary.

Bell, John Henry, M.D., M.R.C.S., Consulting Medical Officer, Bradford Infirmary; Surgeon, Bradford Eye and Ear Hospital.

Caiger, Frederick Foord, M.D., B.S., M.R.C.P., D.P.H., Medical Superintendent and Lecturer on Infectious Diseases, South-Western Fever Hospital, Stockwell.

Calmette, Albert, M.D., Director of the Pasteur Institute of Lille, Professor of Bacteriology and Experimental Therapeutics to the Faculty of Medicine of Lille.

Copeman, Sydney Monckton, M.D., M.R.C.P., D.P.H., Medical Inspector to H.M. Local Government Board, Whitehall; Lecturer on Hygiene and Public Health in the Westminster Hospital School of Medicine.

Davidson, Andrew, M.D., F.R.C.P.Ed., late Visiting and Superintending Surgeon, Civil Hospital, and Professor of Chemistry, Royal College, Mauritius.

Fayrer, Sir Joseph, Bart., Surgeon-General, K.C.S.I., LL.D., M.D., F.R.S., F.R.C.P., late President Medical Board, India Office.

Firth, Robert Hammill, Surgeon-Major, F.R.C.S., D.P.H., Assistant Professor of Hygiene in the Army Medical School at Netley.

Griffiths, Joseph, M.D., C.M., F.R.C.S., Surgeon to Addenbrooke's Hospital, Cambridge.

Guillemard, Francis Henry Hill, M.D., F.L.S., etc., late Lecturer on Geography to the University of Cambridge.

Hart, Ernest, D.C.L., M.R.C.S., Editor of the *British Medical Journal.*

Hutchinson, Jonathan, M.D., LL.D., F.R.C.S., F.R.S., Consulting Surgeon to the London Hospital; Senior Surgeon to the Hospital of Diseases of the Skin, Blackfriars; Consulting Surgeon, Royal London Ophthalmic Hospital.

Lafleur, Henri A., M.D., Assistant Professor of Medicine and Associate Professor of Clinical Medicine, M'Gill University; Physician to Out-patients, Montreal General Hospital.

MacCombie, John, M.D., C.M., Superintendent of the Brook Hospital, Shooters Hill, formerly of the South-Eastern Small-pox Hospital.

MacLeod, Kenneth, Brigade Surgeon Lieutenant-Colonel, M.D., LL.D., F.R.C.S.E., late Professor of Surgery in the Medical College of Calcutta.

McFadyean, John, M.B., C.M., B.Sc., F.R.S.E., Principal and Professor of Comparative Pathology and Bacteriology in the Royal Veterinary College.

Manson, Patrick, M.D., LL.D., F.R.C.P., Physician to the Seamen's Hospital, Albert Dock Branch; Lecturer on Tropical Diseases to St. George's and Charing Cross Hospitals.

Martin, Charles James, B.Sc., M.B., M.R.C.S., Professor of Physiology in the University of Melbourne.

Martin, Sidney, M.D., F.R.C.P., F.R.S., Fellow and Professor of Pathology of University College; Assistant Physician, University College Hospital; Assistant Physician, Brompton Hospital for Diseases of the Chest.

Moore, J. W., M.D., M.Ch., F.R.C.P.I., Physician Meath Hospital and County Dublin Infirmary; Professor of Practice of Medicine, R.C.S.I.; Consulting Physician, Fever Hospital, Cork Street, Dublin; Diplomate in State Medicine, Trin. Coll. Dubl.

Notter, Lane, M.D., M.Ch., Professor of Military Hygiene in the Army Medical School, Netley.

Oliver, Thomas, M.D., F.R.C.P., Physician to the Newcastle-upon-Tyne Infirmary, and Professor of Physiology in the University of Durham.

Osler, William, M.D., F.R.C.P., Professor of Medicine in the Johns Hopkins University, and Physician-in-Chief to the Johns Hopkins Hospital, Baltimore.

Rolleston, Humphry Davy, M.D., F.R.C.P., late Fellow of St. John's College, Cambridge; Assistant Physician and Lecturer on Pathology to St. George's Hospital; Assistant Physician to the Victoria Hospital for Children.

Smith, Eustace, M.D., F.R.C.P., Physician to the East London Hospital for Children, and to the City of London Hospital for Diseases of the Chest.

Stirling, Edward Charles, C.M.G., M.D., F.R.S., F.R.C.S., C.M.Z.S., Director of the South Australian Museum, late Senior Surgeon to the Adelaide Hospital, and Lecturer on Biology in the University of Adelaide.

Verco, Joseph Cooke, M.D., F.R.C.S., Lecturer on Medicine in the University of Adelaide, late Senior Physician to the Adelaide Hospital, South Australia.

Williams, Dawson, M.D., F.R.C.P., Fellow of University College, London; Physician to the East London Hospital for Children.

Woodhead, German Sims, M.D., C.M., F.R.C.P.Ed., F.R.S.E., Director of the Research Laboratories of the Conjoint Board of the Royal College of Physicians and Surgeons.

ERRATA IN VOL. I.

Page 135, Sect. iv., line 7, *for* "J. of Pathol." *read* "J. of Physiology."

Page 503, *for* "(29) Amœbic Dysentery" *read* "(29) Dysentery," *and* "(44) Amœbic Dysentery" *to follow* "(43) Blackwater Fever."

Page 503, *for* "(19) Rubeola" *read* "(19) Rubella."

In order to avoid frequent interruption of the text, the Editor has only inserted the numbers indicative of items in the lists of "References" in cases of emphasis, where two or more references to one author are in the list, where an author is quoted from a work published under another name, or where an authoritative statement is made without mention of the author's name. In ordinary cases an author's name is a sufficient indication of the corresponding item in the list.

INFECTIVE DISEASES OF CHRONIC COURSE

15. TUBERCULOSIS 16. LEPROSY 17. ACTINOMYCOSIS

TUBERCULOSIS

Definition. — Tuberculosis is a chronic febrile disease, produced by the bacillus tuberculosis. It occurs as a natural disease in human beings and some of the domesticated animals, but, so far as is known, does not occur in wild animals. It is widely prevalent in the human race and in cattle. One-seventh of mankind die of tuberculosis, and the prevalence in cattle may be stated as varying from 10 to 20 per cent of all cows.

Bacillus Tuberculosis (Koch, 1882).—The bacillus which is the cause of tuberculosis is a parasitic, and not a saprophytic, micro-organism. In nature, so far as is known, it grows only in the bodies of animals affected by the disease. Outside the body it can be cultivated in specially prepared media, but it does not occur naturally in any particular soil or medium.

It consists of slender rods, varying in length between 1·5 and 3·5 μ. They are often bent, and when long may present a beaded appearance. This beaded appearance is due to the presence of clear areas in the rod, which were at first considered by Koch to be spores. There is, however, no evidence that the bacillus forms spores; and it is improbable that it does so.

Reaction to Stains.—The bacillus behaves in a characteristic manner to some of the aniline dyes, and is thus distinguishable from all other micro-organisms except that of leprosy. It takes up the stain of fuchsin and of gentian violet when these are dissolved in an alkaline liquid, or in one containing carbolic acid or aniline. The colour is not removed by mineral acids up to 25 per cent or by alcohol. The most convenient method of staining tubercle bacilli, whether in the sputum or in tissues, is to use a solution of fuchsin dissolved in carbolic acid, as follows:—Fuchsin 1 gramme, alcohol 10 c.c., 5 per cent solution of carbolic acid up to 100 c.c. The preparation is stained for five minutes to a quarter of an hour in this solution, which is warmed till the steam rises, and is then placed in a 25 per cent solution of sulphuric acid until it is decolorised. As a rule this takes a minute or two, but no harm comes to the preparation if it be left a quarter of an hour in the acid. It is then well washed in distilled water, to get rid of the excess of acid, and as a rule it takes on a faint pink tinge. It must now be counter-stained, preferably by a dilute solution (1 to 2 per cent) of methylene blue. Half to one minute is sufficient for this, and after washing in water, the preparation is ready to be mounted. Specimens of sputum dried on a cover-glass may be stained for five minutes in the fuchsin solution, and half a minute in the methylene blue solution, and mounted, after drying, in Canada balsam, or examined in water. For sections of tissues it is best to stain for fifteen minutes in the warm fuchsin solution, after sticking the preparation on the cover-glass or slide. After counter-staining with methylene blue the section is to be dried with fine filter paper, washed rapidly with alcohol, clarified with xylol, and mounted in xylol balsam. By this method the tubercle bacilli are the only micro-organisms stained red, the other organisms which may be present being decolorised by the acid. These, as well as the ground tissue and cells, are stained blue by the methylene blue.

Gentian violet may be used as a stain for the tubercle bacillus, the specimen being fixed with iodine solution and decolorised with alcohol; bismarck brown, eosin, or vesuvin may be used as a counter-stain. This method gives very good results; but the other is more generally serviceable.

Cultivation of the Bacillus.—The bacillus tuberculosis grows best at the temperature of the body. At low and high temperatures its growth is impeded or completely stopped. The range of temperature at which it will grow is between 28° and 42° C. It may be artificially cultivated by using various media. Solidified blood serum is the best for obtaining the bacillus from the tissues, and was the one used by Koch in his first research. When the surface of the solidified blood serum is inoculated with pure tuberculous material, and the tubes are kept at a temperature of 38° C., no growth appears as a rule during the first week, but in from 7 to 10 days white specks are seen on the surface of the serum which, when examined under the microscope, appear as dry flakes. The growth extends in a circular manner from these foci, and the older growths, while still remaining dry, become crinkled and folded, presenting a very characteristic appearance. The growth is very slow, and it may be weeks before it covers a large area of surface.

The bacillus may also be grown on other solid media, such as blood serum containing gelatine, or peptone-agar containing 4 to 8 per cent of glycerine. On peptone-agar without glycerine the bacillus does not grow. Glycerine not only aids the growth in solid media, but, in the percentage above-mentioned, stimulates the bacillus to grow in liquid media, as, for example, in peptone-bouillon. It can also be grown on potato in sealed tubes (Pawlowsky). Grown on solid media the bacillus is apt to lose its virulence. In liquid media containing glycerine the virulence may be maintained for a somewhat longer time.

The action of direct sunlight is fatal to the bacillus, as was first shown by Koch. This has been confirmed by subsequent observations. Oxygen is necessary for the growth of the bacillus.

Chemical Products.—But little is known of the chemical products which are produced by the bacillus tuberculosis in its growth. Koch separated a substance called "tuberculin," which has a specific action. This substance, which has not been obtained in a pure state, is prepared by growing the bacilli for six to eight weeks in a slightly alkaline veal broth, containing 1 per cent of peptone and 4 to 5 per cent of glycerine. After cultivation the liquid is evaporated to a tenth of its bulk, and filtered through porcelain; this filtrate is the liquid which is called tuberculin: it contains 40 to 50 per cent of glycerine, which keeps it aseptic. By adding alcohol the active principle is precipitated in an impure state. This differs from most of the other bacterial products in resisting a high temperature, even the boiling-point of water. The specific action of tuberculin is shown in the fact that it produces a great rise of temperature in men and animals the subject of tuberculosis, while similar small doses injected into healthy individuals produce no rise of temperature. The fever ensues from 6 to 12 hours after the injection, and lasts a varying time—in some cases 24 hours, in others 48, or even longer. It may produce in a tuberculous individual or animal great bodily depression, leading to collapse. It was introduced as a curative agent, but its use is now limited to the diagnosis of tuberculosis in cattle. Its continued injection in a case of tuberculosis leads to dissemination of the disease; so that whereas at first the disease may be limited to the lungs, after a course of tuberculin the patient may die with disseminated lesions in various organs of the body. The same observation has been made in cattle. Tuberculin, therefore, is a specific product of the bacillus, inasmuch as it has a specific action, namely, that of producing fever, and so acting on the local processes in tuberculous individuals that the disease becomes disseminated.

Of the chemical products which the bacillus actually produces in the body practically nothing is known. There may be a substance or substances producing caseation, and there must be a chemical body which produces the fever. These, however, have not been isolated. Prudden and others found that when injected into an animal the dead bacilli produced local inflammation and hyperplasia, which ended in fibrosis. There was, however, no spread of the disease. This effect was ascribed to the presence of a hypothetic body—protein—which has been supposed to exist in the bodies not only of the tuberculosis bacillus, but of other micro-organisms.

Pathological Effect of the Bacillus.—When injected into animals the bacillus produces lesions, and the disease which is now to be studied as tuberculosis. First a local lesion is produced, and from this the disease spreads to the glands and organs of the body (see Pathology of Tuberculosis, p. 15). This statement applies to the bacillus tuberculosis separated from the lesions of the disease in human beings and in all affected animals except birds.

Avian Tuberculosis.—Tuberculosis is found as a natural disease in fowls, pheasants, pigeons, turkeys, peacocks, and other birds which are kept in captivity. The bacillus, which has been separated from the lesions produced, differs in some respects from that found in cattle and in human beings. It is stained in the same manner by fuchsin, and may be grown in the same media as the human or bovine bacillus tuberculosis; but it differs in that it is more vigorous and resistant.

This bacillus grows luxuriantly at a temperature of 43° C., at which the human and bovine bacillus tuberculosis will not grow. The appearance of the cultures is also different; instead of being dry and crinkled they are moist and soft. The results of inoculation are also different: in guinea-pigs and rabbits the inoculation of the human bacillus produces a spreading disease, which eventually invades most of the organs of the body, whereas the bacillus of avian tuberculosis produces in the guinea-pig a local disease which does not spread to the internal organs. Dogs are immune to avian tuberculosis, but they can be infected by large doses of human and bovine tuberculosis: on the other hand, the hen cannot be infected with human or bovine tuberculosis. Although from these statements it would appear that avian tuberculosis is not the same disease as bovine or human tuberculosis, yet there are some facts which show that it is a modified form of that disease. Thus, it has been shown that inoculation of human tuberculosis into fowls sometimes succeeds, and when it does, re-inoculation is also successful. Moreover, when a slight lesion is produced in guinea-pigs by the inoculation of avian tuberculosis material, the transmission from guinea-pig to guinea-pig results in the typical spreading disease which is observed after the inoculation of human tuberculosis (Nocard). This, perhaps, is even more evident in rabbits than in guinea-pigs.

Lesions produced by the Bacillus Tuberculosis.—Wherever the bacillus tuberculosis grows in the animal body it produces a lesion which has certain definite characteristics; and it is necessary to study this lesion before we consider the distribution of the disease in individual cases of tuberculosis, or its spread. The lesion consists of small whitish nodules, which may be more or less numerous, and by their aggregation may form large masses. Each of the small primary lesions is called a granulation or a miliary tubercle. Either singly or fused into masses they undergo definite changes by which their original structure is completely lost: the chief of these is caseation or necrosis—fatty degeneration of the cells forming the tubercle. The caseated matter may soften or be discharged, or may calcify. The second change which occurs in the tubercle is fibrosis, which is frequently associated with pigmentation. All these changes are degenerative. The primary lesion, the gray granulation, is composed of cells, and is throughout its whole extent nonvascular; a point of some importance in the explanation of the degenerative changes which occur.

Microscopical Appearances.—According to the size of the cells which compose the gray granulation a small-celled and a large-celled tubercular nodule may be distinguished. The small-celled granulation consists of mononucleated cells, derived from the leucocytes of the blood and lymph.

The large-celled tubercle consists in the main of so-called epithelioid cells—cells which have a definite outline, are roughly ovoid, and are often compressed. These cells, especially in the early stages of the formation of the tubercular nodule, frequently show the phenomenon of karyo-mitosis, that is, a division of their nucleus with a star-shaped figure at each end. Karyo-mitosis is also observed in the endothelial cells of the blood-vessels. Giant cells are present both in small-celled and large-celled tubercle; they vary in size, and present the common characteristic of a large number of nuclei at the periphery. The nuclei are oval, and usually are not distributed evenly round the periphery of the cell. In most cases they are collected to one side, and they are not unfrequently two rows deep. Between the epithelioid cells there is sometimes a fine reticulum, as in lymphoid tissue, and there is a serous or fibrinous exudation from the blood-vessels. The number of small cells present in the tubercular nodule varies; and, according to Baumgarten, the migration of leucocytes occurs earliest when there has been an injury to the tissue. They collect round the periphery of the tubercle. Baumgarten considers (and his view has been accepted by most pathologists, including the German school) that the first change occurring in the formation of the gray granulation is the proliferation of the fixed tissue cells, forming the so-called epithelioid cells. In the lung, for example, it is the cells of the alveoli which form the tubercle; in the liver it is the hepatic cells; in the kidney the renal cells; and the migration of leucocytes is a subsidiary phenomenon in the formation of the nodule, occurring at a later period. This view is combated by Metschnikoff, who considers that the tubercular nodule "is composed of a collection of phagocytes mesodermic in origin, which move towards the spot where the bacilli are situated, and englobe them." Thus, in the liver, if the tubercular nodule be examined shortly after its formation in experimental tuberculosis, it is found that the epithelioid and giant cells are formed by the large mononuclear leucocytes and cells derived from the vascular endothelium, and that the hepatic cells take no part in the formation of the tubercle. He states the same facts with regard to the lungs. The leucocytes which are present in the tubercular nodule are almost all mononuclear. Polynuclear leucocytes are present, and take into their substance tubercle bacilli, but they soon die, being eaten by the mononuclear phagocytes (macrophages). These macrophages can destroy the tubercle bacilli.

Retrogressive Changes of the Tuberculous Lesion.—*Caseation.*—The first and chief retrogressive change which occurs is caseation; as the tubercle is a non-vascular collection of cells, and tends to unite with similar tubercles in the neighbourhood, thus forming a large non-vascular mass, death of the parts farthest removed from the blood-vessels would be likely to occur, as in an infarct, where the blood-supply to a portion of the tissue has been cut off by blocking of the artery supplying it. It is also quite possible that caseation is a specific action of the bacillus tuberculosis itself. It may be that a chemical substance is secreted by the bacillus which kills the cells; in any case it is certain that many of the cells which contain tubercle bacilli die and become completely degenerated. This is seen even in very small miliary granulations. According to Baumgarten, the death of the leucocytes occurs first, and then that of the epithelioid cells; while the giant cells are themselves in a state of partial necrosis, so that they do not undergo division into daughter cells, as the presence of numerous nuclei in their substance would suggest. Metschnikoff considers that the greater part of the tubercle being composed of leucocytes—that is to say, of mesodermic cells—the polynuclear leucocytes are the first to die, being killed by the bacillus and then eaten by the mononuclear leucocytes, which in their turn resist the action of the bacillus for a longer period, and may eventually either kill the bacillus or be killed by it.

Microscopical examination shows very various appearances. In the early stages of the death of the cell the protoplasm becomes granular and fatty, and finally breaks down; the nuclei lose their oval form, becoming shrivelled and broken up into irregular masses, which even a long time after the cell has disappeared take up the stains of logwood and methylene blue. Where a number of cells of the tubercle have undergone caseation, forming a mass of perhaps a quarter of an inch in diameter in the centre of the caseated area, no structure is apparent; a few darkly-stained spots represent, perhaps, the remains of the nuclei, and the fine granules are chiefly fatty matter. Towards the periphery of the caseated patch, however, nuclei are seen, which present a shrivelled appearance, and are commencing to break up into small particles. Around the caseated area the appearances vary according to the stage of the tuberculosis. There is more or less fibrosis, with infiltration by leucocytes; and there may be outlying tubercular nodules which present the appearances previously described. The caseated nodules by joining together produce large tuberculous masses, especially in bovine tuberculosis. The softening of the caseated matter, and its expulsion through the bronchial tubes, may result in the formation of a cavity in the lungs; or a similar process in a mucous membrane may result in the formation of an ulcer.

Calcification is a retrograde change in the tubercle which occurs after caseation. The actual deposition of the phosphate of lime, which is the chief component of the calcareous matter, has been attributed to the diminution in the amount of carbonic acid at the spot where it occurs. It is observed in old tubercular lesions in man, cattle and pigs, but not in guinea-pigs or in rabbits, and very rarely in the horse. It occurs, therefore, in animals in which tuberculosis may take a very chronic course. It is difficult to state the earliest period of the tubercular lesion at which calcification may occur, but in experimental tuberculosis in the pig it has been observed as early as 106 days after infection.

Microscopically, calcareous matter is seen deposited in the form of granules in the cells. It is, however, not infrequently in the form of a nodule, which by treatment with acid shows concentric rings, as in a renal calculus (Schuppel). In experimental tuberculosis in the Algerian rat (Meriones), an animal which is very refractory to the disease, Metschnikoff found bodies similar to those described by Schuppel as occurring in human tuberculosis, and observed in various specimens their mode of formation. They are, in short, the results of the degeneration of the tubercle bacillus in the interior of the giant cell. In the course of the disease, which is extremely slow in its progress, the bacilli become surrounded within the cell by concentric layers of an amorphous, colourless substance which eventually becomes impregnated with phosphate of lime. The concentric membranes are not affected by alkalies, and do not give a red colour with Millon's reagent; but they are dissolved by concentrated acids. They appear to be composed of a substance similar to that enveloping the tubercle bacillus. The bacillus inside the concentric layers degenerates, so that although at first it takes the stain of fuchsin or gentian violet, in the later stages it does this very imperfectly, and finally not at all. These observations appear to show that the concentric bodies are really part of the products of the fight between the bacillus and the giant cell.

Calcification is one of the modes by which tubercle heals, as the completely calcified lesion is no longer infective.

Fibrosis is a second mode of healing of the tubercular nodule. It occurs at the periphery of the nodule, and is secondary to the inflammation set up by the presence of the gray granulation. It occurs in chronic tuberculosis, and is very evident in cases where the tissue has been injured. Thus, in the local lesion following the injection of tuberculous material under the skin, fibrosis is extensively produced; also in parts which are exposed to friction, as in joints, when they are infected by tuberculosis. Pigmentation frequently accompanies fibrosis, and is due to the exudation of hæmoglobin from the congested blood-vessels. It may occur around the miliary granulation, as when these have been surrounded by a zone of congestion. Thus in the peritoneum and lung it is not infrequently observed that a small gray granulation is surrounded by a bluish ring of pigment and by fibrous tissue.

Lesions of various Parts as they occur in Tuberculosis.—The tuberculous lesion has the structure which has just been described, in whatever part of the body it may be found; but the appearances vary with the association of the early lesions with the degenerative changes present, and also with coincident non-tubercular lesions.

The Lungs and Pleura.—In the lungs tuberculosis may occur either in the acute or caseous miliary form, in the chronic form, or in a form in which fibrosis is the chief element.

(*a*) *Acute Miliary and Caseous Tuberculosis.*—This is secondary to a primary focus elsewhere in the body. The naked eye appearances are those of miliary granulations scattered more or less uniformly throughout the substance of the lung, in some parts aggregated into masses—the so-called racemose patches—but in most parts discrete. Some of the granulations may show central caseation, and when the granulations are large and caseated the condition is called caseous tuberculosis. The lung tissue itself is generally congested, and there may be distinct zones of congestion round the tuberculous nodules, especially when they are found beneath the pleura. Patches of collapse and emphysema are also frequently observed.

(*b*) *Chronic Pulmonary Tuberculosis.*—The usual appearances of tuberculosis of the lungs are those which are found at death in chronic pulmonary tuberculosis. The most advanced stage of the disease is at the apex of the lung, and here is found a cavity varying in size and shape, and surrounded by fibrous pigmented tissue, showing its chronic character. In very old cavities the wall is smooth-lined, but in more recent (although still chronic) the walls may be lined by a cheesy material, and numerous cavities may be joined together, forming sinuous tracts in the upper part of the lung. Below the cavity, in the upper lobes and to a varying extent in the lower, the more recent deposits of tubercle are seen, consisting of miliary granulations, uniting into racemose patches and commencing to degenerate; or quite recent cavities, full of a soft, yellowish, cheesy material formed by the complete degeneration of the racemose patch. The racemose patches are not only in the substance of the lung, but near the surface, on which they may form a slight projection; on section they may be wedge-shaped like an infarct, showing that they were formed either by infection through an end artery or by inhalation through a bronchial tube. Both lungs may be affected, and the extent of the recent tuberculosis is greater in the lung which was first affected than in the other. In this form of tuberculosis, therefore, there are evidences of a chronic lesion which has lasted a long time—it may be years—with a subsequent acute outbreak of tuberculosis below the chronic lesion, which may be the actual cause of death, and is constantly observed to occur during life. The bronchial glands also are usually affected by tuberculosis in the manner presently to be described.

The pleura may be affected in two ways: either as a result of an extension of the form of disease described above; or primarily, although this is rare in man. Tuberculosis of the pleura in its early stage is shown, as a rule, by the growth of miliary granulations beneath the pleura, and subsequently by the development of a large amount of fibrous tissue; in some cases, however, the tuberculosis leads to pus formation and the production of an empyema. Some cases of empyema that occur in chronic pulmonary tuberculosis are probably not directly tubercular, although this is not quite clear; but in the majority of cases the pus formation must be ascribed directly to the presence of the tubercular lesions in the lung.

Besides non-tubercular empyema there are other associated lesions in chronic pulmonary tuberculosis. Pneumonia may occur, as in a healthy lung; and in patients dying of chronic pulmonary tuberculosis broncho-pneumonia and collapse are frequently found situated between the tuberculous lesions. The occurrence of broncho-pneumonia in the course of advancing tuberculosis, or just before death, is perhaps to be ascribed to the inhalation of irritant bodies in the sputum, and is not a tubercular infection, for if it were it would caseate, which it never does.

Dry pleurisy, occurring in the course of tuberculosis, is usually tubercular, and is associated with the presence of tubercles on the pleura; effusion may result, the liquid of which may not contain tubercle bacilli; but even in this case the pleurisy is usually tubercular.

Secondary pus infection of the lung may occur, usually in cavities; that is, the cavity may be infected by pus cocci. Gangrene may follow, and this is associated with thrombosis of the vessels and infection of the dying tissue by micro-organisms which are inhaled through the bronchial tubes.

(*c*) *Caseous Pneumonia.*—Somė of the cases described under the heading Caseous Pneumonia are tubercular. They present a very different appearance from that which has been described as occurring in chronic tuberculosis. There is more or less uniform consolidation over a greater or less area of the lung, and in what appears to be the less advanced stage of the disease the surface is granular on section, presenting a whitish yellow appearance. In other parts there is caseation. The diagnosis in such a case may be doubtful until the specimen is submitted to microscopical examination, when definite tubercles will be seen surrounded by consolidated lung, and containing giant cells and tubercle bacilli. Tubercular pneumonia occurs either as secondary to a primary focus in the apex of the lung or to a primary focus elsewhere.

(*d*) *Fibroid Tuberculosis.*—Fibroid tuberculosis occurs in three forms —as a localised nodule at the apex of the lung, as fibrosis of an area of lung affected by miliary tuberculosis, or as a slowly spreading fibrosis, associated with very chronic tuberculosis, lasting over many years. Fibrosis is a feature in all cases of chronic tuberculosis of the lungs, and is the mode by which the tubercular focus is encapsuled and infection of neighbouring or other parts prevented. The fibroid patches that are not uncommonly found at the apex of the lung are a form of what is called retrograde or obsolescent tubercle. Nodules varying in size from half an inch to an inch in length are seen, which on section show a periphery formed of dense fibroid and pigmented tissue, frequently puckering the surface of the lung; and a centre, which is usually calcareous and may contain caseated matter. Where there is caseated matter tubercle bacilli are to be found as a rule, although they are scanty and stain badly with fuchsin, showing that they are degenerated. Such fibrous nodules are but rarely infective. In three cases in which they were removed from the lung antiseptically, and introduced subcutaneously into guinea-pigs, no tuberculosis resulted. Fibrosis of a portion of the lung, usually the upper part, which has been affected with miliary tuberculosis without caseation, is not a common event; but it is sometimes observed in post-mortem examinations, when, as a rule, recent tubercular lesions are found elsewhere. The part of the lung affected presents a dark appearance, is somewhat contracted, and is very tough: microscopically the alveolar structure is almost completely destroyed by the interstitial fibrosis, and the places where miliary granulations existed are recognised by the indistinct appearance of nodules completely transformed into pigmented fibrous tissue.

The form of disease to which the term fibroid tuberculosis is applied clinically is that in which, as a result of a very slowly progressing disease, extending perhaps over many years and usually limited to one lung, there is extensive formation of fibrous tissue round the tubercular lesion or cavity, which fibrosis spreads into the rest of the lung. Associated with it, and as a result of the contraction of the fibrous tissue, there is extensive bronchiectasis. At the time at which the lung is examined post-mortem there may be little or no evidence that it is tubercular, inasmuch as all caseous material may have disappeared, and the lung be one series of cavities, some of which are tubercular, but most of which are bronchiectatic; these are surrounded by dense strands of connective tissue in which no trace of tubercle is discoverable. There is no other primary chronic disease that produces this condition of lung except tuberculosis, the fibrosis and bronchiectasis resulting from pneumonia being localised, and not as a rule extending beyond the original limits of the acute disease.

The peritoneum is affected in two forms: either as part of a general disease, or as a result of intestinal infection. When tubercular peritonitis is part of a general tuberculosis the appearances are those of numerous miliary granulations present over both the visceral and parietal peritoneum. They vary in number, and, if of long standing, are surrounded by a zone of pigment. Chronic tubercular peritonitis is a result of intestinal tubercular infection, but there may or may not be a local lesion in the intestinal mucous membrane. In well-marked tubercular ulceration of the intestines there is very frequently a deposit of miliary granulations in the peritoneum which is congested at the spot, or covered with a little lymph. But, in children especially, intestinal tubercular infection may lead to a generalised peritonitis. This is associated with enlargement and caseation of the mesenteric glands (tabes mesenterica), showing that the course of infection was from the intestines. The peritoneum itself is no doubt in the early stages covered with miliary granulations, although this stage of the disease is not seen post-mortem. When the disease becomes developed, the miliary granulations have greatly increased in number, and have united, especially in the great omentum; and the great fibrosis resulting from the presence of the tubercles produces bands of thickened peritoneum stretching across the abdomen, binding the intestines together and frequently distorting them. As in the pleura when it is infected by tuberculosis, effusion may occur, which may be either a nearly clear straw-coloured liquid or pus. The pus may be bound down by adhesions forming a localised abscess.

Meninges.—The pia mater is affected with acute miliary tuberculosis, either as part of a general tuberculosis, or secondary to an active focus elsewhere—for example, the joints, lungs or intestines. The granulations which occur are very small; they are seen in the interpeduncular space, and are situated alongside of the vessels running into the Sylvian fissure. They are present also in the lymphatic sheaths of the vessels which enter the brain from the pia mater, and they may extend backwards from the interpeduncular space into the part of the membrane lying in the transverse fissure of the brain. Pus is not infrequently present in the interpeduncular space, and is in most cases limited to the base of the brain. The formation of pus is due to the action of the tubercle bacillus itself; in cases of tubercular meningitis there is usually no secondary infection by pus cocci.

In the brain the form tuberculosis takes is that of nodules varying in size from a line to an inch in diameter, almost completely caseated, and usually surrounded by a capsule of unpigmented fibrous tissue. The nodules are quite discrete, and the caseated matter on section presents a peculiar greenish yellow appearance. It is quite firm, and tubercle bacilli are usually to be found. In rare cases similar nodules may be found in the spinal cord. The parts of the brain in which the tubercular nodule is found vary. It is always in the substance, and may be present in the hemispheres, in the commissures, cerebellum, pons or medulla.

Alimentary Tract.—Tubercular lesions in the intestines may be primary or secondary, and may occur in the small or large gut. Tuberculous ulceration of the pharynx and fauces is extremely rare, and occurs only in cases where the lungs are affected. In the œsophagus and stomach tuberculosis is practically unknown. Rarely a small tubercular ulceration may be found in the stomach, but only in advanced cases of tuberculosis, and where the secretion of hydrochloric acid is deficient. In the first part of the duodenum also, of which the contents are acid, tubercular ulceration is extremely rare; but from the duodenum to the ileo-cæcal valve tuberculous ulceration is increasingly frequent, the chief parts of the mucous membrane in which it occurs being those in which the Peyer's patches are most numerous. Ulceration of the large gut may occur independently of that in the small gut, or both may be associated; but the large gut is not so frequently affected alone as the small. As elsewhere, the first sign of tuberculosis in the mucous membrane is seen in the deposit of nodules which coalesce and caseate, finally leading to necrosis of the superficial tissue and leaving an ulcer. The nodules may be present either in the deeper part of the mucous membrane or quite near the surface of a Peyer's patch. Both deep and superficial ulcers are thus formed. A fully formed tubercular ulcer of the small intestine is not uncommonly transverse to the direction of the gut, but is chiefly characterised by its irregularity, by its thickened edges which are not undermined, and by its base, which is uneven, and shows a deposit of small caseated nodules, which may be situated either in the muscular tissue or in the peritoneum. Perforation of the ulcer may occur, but as a rule this is prevented by adhesions to the neighbouring part of the gut due to the slight peritonitis produced by the ulcer. The result may be to mat the intestines together and to form irregular communications. Perforation in this form occurs almost equally in the small gut and in the large.

Lymphatic Glands.—The early tubercular deposits in the lymphatic glands occur as miliary granulations, which rapidly caseate, unite together, and form the characteristic cheesy masses so frequently seen. This process commonly ends in calcification or fibrosis. In tuberculosis of the glands near the trachea or bronchial tube, and of the superficial glands of the neck, axilla or groin, necrosis of the tissue superficial to the gland may occur, and the caseous contents of the gland be extruded, leaving a tubercular sinus. This frequently occurs in the glands of the neck and sometimes in the bronchial glands.

Bones.—Tuberculosis in the cancellous parts of the bones begins in a manner similar to that already described in other parts, soon leads to the formation of large caseous masses with disintegration of the bony tissue, and not infrequently to the formation of pus. This occurs in the "cold" abscesses that result, for example, from caries of the spine. Here, as in the meninges, the formation of pus is due to the action of the tubercle bacillus itself. The contents of the abscess are thick and ropy, and include numerous pus cells in various stages of degeneration, besides yellowish masses of caseous matter. Tubercle bacilli are with difficulty found in the pus from these abscesses, and sometimes inoculation into animals fails to give a positive result.

Joints.—The deposit of tubercle in the joints occurs in the synovial membrane; it leads to a great thickening due to the increase of gelatinous fibroid tissue, and either to effusion into the joints or to the formation of an abscess. The bones forming the joints are also not infrequently affected by tuberculosis.

The kidneys are affected in two ways: either in the form of miliary granulations, irregularly deposited through the kidney substance, and most numerous in the cortex; or in the form of caseous patches, which are primarily formed in the apex of the pyramids and extend towards the cortex. In this way the whole kidney substance may be destroyed, the large caseous mass formed by the union of caseous masses representing the divisions of the kidney. Before the whole of the kidney substance is destroyed, miliary granulations beginning to caseate are to be seen round the periphery of the caseous mass; that is to say, the primary focus has led to the formation of numerous secondary foci of tuberculosis.

Suprarenal Capsules.—Tuberculosis of these bodies, which is observed in Addison's disease, is usually seen (post-mortem) as a complete caseation of the capsule associated with fibrosis and calcification. Tubercle bacilli are with difficulty found in these cases. Whether the form of Addison's disease associated with fibrosis and atrophy of the capsule be due to a primary tuberculosis of the organ or not, it is impossible to say. As a rule, in these cases no caseation or calcification is observed.

The liver and spleen are affected in a similar manner, viz. in the form of miliary granulations. Tuberculosis of these organs is observed only as secondary to a tubercular focus elsewhere. The granules, especially in the liver, are frequently microscopic only; but they may be a line in diameter, showing a caseated centre. They project from the surface of the organ, and are also present in its substance. In the liver the nodules are never large unless there be some secondary pus infection, as occurs sometimes in tubercular empyema of the right side. Large tubercular nodules are found in cattle and in pigs, but they are very rarely found in the liver of man. In the spleen the irregular distribution of the nodules, as well as their caseation, serves to distinguish them from the enlargement of the Malpighian corpuscles which occurs in Hodgkin's disease. Caseous masses in the liver and spleen are less rare in children than in adults.

In the skin tuberculosis is seen in a very chronic form. as lupus. It is characterised by the same microscopical appearances as those which have been described, and the tendency is to necrosis of the cells and of the superficial tissues, leading to ulceration. Fibrosis is quite subsidiary in the extending disease, although it is well marked in the scarring which results from the healed ulcers.

Pathology.—The anatomical characteristics of tuberculosis, both from the histological point of view and from the manner in which the disease affects individual organs or parts, are but a very small part of the subject of tuberculosis as an infection. Not only must the proof of the bacillus tuberculosis being a necessary factor in the disease be discussed, but the question of the modes of infection, and of the parts affected by these different modes, as well as the spread of the disease in the body from a local focus, must be considered likewise. In connection with this, too, arises the question of the usual source of infection in man, as well as the questions of the effect of dose and virulence of the virus, and of the resistance of the body to its invasion and spread.

The Bacillus Tuberculosis as a Cause of Tuberculosis.—This bacillus has been definitely proved by the experimental method to be a necessary factor in the causation of tuberculosis in the following manner :—

(*a*) The bacillus is found in tubercular lesions both in man and animals. In a particular lesion the bacillus may be absent, having died ; but in one or other lesion of the body of a tuberculous animal, and in nearly all recent tubercular lesions, tubercle bacilli are readily found.

(*b*) The bacillus has been separated from tubercular lesions in man and cows, and from the sputum in man, and obtained in pure cultivation.

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These facts do not rest on any single series of experiments, for since their discovery in 1881-82 by Koch, they have been repeated and confirmed by numerous observers, and receive, indeed, continual confirmation in every pathological laboratory. They serve, then, as the basis of discussion of the pathology of tuberculosis.

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(*d*) From the lesions in the experimental cases in animals the bacillus can be obtained in pure cultivation, living and virulent.

These facts do not rest on any single series of experiments, for since their discovery in 1881-82 by Koch, they have been repeated and confirmed by numerous observers, and receive, indeed, continual confirmation in every pathological laboratory. They serve, then, as the basis of discussion of the pathology of tuberculosis.

Tubercle Bacilli from Human and Bovine Tuberculosis.—The bacilli separated from tubercular lesions in man, in cows and pigs, and in all other domesticated animals except birds, are practically indistinguishable. They have the same appearance microscopically; they react in a similar manner to stains; in artificial cultivation they grow in a similar manner, and when inoculated into animals the disease produced is in all cases alike both anatomically and in its mode of distribution. There are some differences in the manner in which tuberculosis affects the human being and affects the cow; these will be discussed later. The material of bovine tuberculosis is infective to the human being—as, for example, in cases where veterinary surgeons have wounded their fingers in making post-mortem examinations on tuberculous cows, and have subsequently manifested a local tuberculosis in the wound, followed in some instances by pulmonary tuberculosis and death (Nocard). There are also cases in which children have succumbed to tuberculosis produced by the ingestion of the milk from tuberculous cows.

Modes of Infection.—The most satisfactory classification of tuberculosis from the point of view of infection is into that of—(1) local, and (2) generalised. As regards local tuberculosis we have to inquire how the virus entered the body. Thus, the disease may be localised at the point of entrance of the virus, and may remain so for a long period of time; tuberculosis, that is, as it affects an individual, may remain here throughout, and may heal. On the other hand, tuberculosis may be localised in parts far removed from any of the paths by which the virus enters the body—such, for example, as tubercular joint-disease occurring in an individual who apparently has no other tubercular lesion. As examples of local tuberculosis occurring at the seat of invasion of the body, primary pulmonary tuberculosis may be quoted, or intestinal and peritoneal tuberculosis, or tuberculous lymphatic glands in the neck. We speak of generalised tuberculosis when the disease spreads from a focus established in the manner just described; or when it occurs in an individual in whom the local focus may be completely extinguished. The great number of questions which arise in the consideration of these points are for the most part answered by the results of experimental tuberculosis in animals. In the investigation of modes of infection in man, whether of the sanitary surroundings or of the distribution of the lesions present in the body at death, it has been most difficult to determine the mode of infection in tuberculosis; in many cases it is evident that the virus has been inhaled and local tuberculosis of the lungs has resulted, or that it has been swallowed and intestinal tuberculosis has resulted; yet for the explanation of tuberculosis localised in parts remote from the channel of infection but few facts are forthcoming.

Experimental tuberculosis is of the highest importance in the study of the disease; inasmuch as the effects of dosage, virulence of the virus, and resistance of the body to the infection can be gauged. The effect of the resistance of the body is readily determined by observing the effects of the same dose of virus in susceptible and refractory animals—in guinea-pigs and rabbits, for example, which are susceptible animals, and in dogs and some species of rats which are refractory animals.

Experimental Tuberculosis.—The following points will be considered in discussing experimental tuberculosis:—

(*a*) Variations in the intensity or rapidity of the disease after inoculation or feeding or inhalation of tuberculous material.

(*b*) The virulence of different forms of tuberculous material.

(*c*) The varying effects of dose on the extent of the tuberculosis produced.

(*d*) The formation of a local lesion or not at the seat of entrance of the virus into the body.

The resistance of the body to the invasion of the disease—that is, natural immunity—will not be considered in the following discussion, which relates only to animals susceptible to the disease—namely, guinea-pigs, rabbits, calves and pigs. Calves and pigs are both subjects of natural tuberculosis; but in guinea-pigs and rabbits tuberculosis is unknown outside the laboratory. These two animals, indeed, especially the guinea-pig, kept under hygienic conditions, serve as excellent and accurate tests of the infectivity of any particular tuberculous material.

Inoculation Experiments.—In guinea-pigs inoculated subcutaneously in one or other groin by virulent tuberculous material, as early as nine days after inoculation a local lesion is seen which, on microscopical examination, may be recognised as tuberculous. The inguinal glands become tuberculous in from seven to fourteen days, and about the third week after inoculation the disease spreads to the internal lymphatic glands, always affecting the lumbar glands, and usually affecting the cœliac glands before it spreads to the liver and spleen. Spreading to the thorax (which it does about the fourth week) the posterior mediastinal and bronchial glands are first affected; and subsequently, about the fifth week, the lungs. The mesenteric glands are affected only in very advanced tuberculosis following inoculation. The suprarenal bodies and the kidneys are never found affected by the disease.

If the tuberculous material be inoculated in both groins the disease is developed on both sides—that is, both inguinal and both lumbar lymphatic glands become affected; whereas if one side only be inoculated the lumbar and inguinal glands of the other side do not become tuberculous, although the lumbar glands may become so in the later stages of advanced tuberculosis in the guinea-pig.

The intra-peritoneal inoculation of virulent tuberculous material produces an intense tubercular peritonitis, with great thickening of the omentum and the deposit of miliary tubercules over both the parietal and visceral peritoneum: this is evident in from ten to fourteen days after inoculation. In fourteen days tubercle of the lumbar, cœliac, anterior and posterior mediastinal lymphatic glands may be evident, and, if very virulent material be used, tubercle of the liver and spleen or even of the lung. In sixteen to twenty-one days practically every organ of the body may be affected, except the gastro-intestinal tract, and, in the guinea-pig, the suprarenal capsule and kidney. The mesenteric glands become affected at a very late stage of the tuberculosis, and ulcers of the intestines are never produced by the inoculation of tuberculous material wherever introduced.

Inoculation into the interior chamber of the eye produces, in seven to ten days, a local tuberculosis, which then spreads to the neighbouring lymphatic glands, and finally to the lungs and other organs of the body.

Important as are the results of the inoculation of virulent tubercular material, of greater importance is the effect of the inoculation of non-virulent material—such, for example, as is not unfrequently met with in meat removed from tuberculous animals, and in milk given by cows with tuberculosis of the udder—as well as with virulent material, such as highly infective milk, which has been diluted.

It may be said that the inoculation of sputum from cases of pulmonary tuberculosis in man, as well as of material obtained from recent and progressing lesions of the disease, produces the effects which have just been described, namely—(1) a local lesion; (2) a spread of the disease to the lymphatic glands nearest the local lesion; (3) the invasion of the solid organs of the body.

Sputum, no doubt, has a varying infectivity, dependent on the character of the lesion which produces it, whether, that is, it contains a large number of living tubercle bacilli or not. Not many experiments, however, have been performed from this point of view. Of great importance in human pathology is the result of inoculating the meat and milk from tuberculous animals into guinea-pigs and rabbits. The milk from a cow with tuberculosis of the udder may, as I have shown elsewhere, be highly infective, or only slightly so; and the infectivity is due to the presence of tubercle bacilli in the milk, coming, as in the sputum of pulmonary tuberculosis, from the breaking down of tuberculous lesions. The meat from tuberculous cattle may also be highly or only slightly infective; but in this case the infectivity does not depend on the presence of tuberculous lesions in the muscular tissue itself, but on the contamination of the meat, during its removal, by or from the tuberculous lesions present in the carcase.

The effects, therefore, which will be described as resulting from the inoculation of meat and milk into animals vary with the dose of the virus present in the inoculated material; inasmuch as, apart from the dose, the virulence of the bacilli in a particular lesion cannot at present be gauged. In a highly infective disorder, such as anthrax, where death follows inoculation in twenty-four or thirty-six hours, the dosage is not of so much importance as the virulence or vitality of the bacillus. That is, speaking broadly, twice the fatal dose of material containing anthrax bacilli will not produce a greater effect in a guinea-pig than a smaller dose. But in the case of anthrax bacilli the virulence may vary greatly, and produce corresponding effects in the animal body. With tuberculosis, however, dosage is of greater importance, inasmuch as the larger the dose, within limits, the greater the degree of tuberculosis produced in a susceptible animal. For tuberculosis is essentially a chronic disease, one in which the infective agent grows slowly; therefore with a small number of bacilli the body is more likely to resist their invasion and to restrict their action to the seat of inoculation, whereas with a large dose this defensive action is not so effective. Take, for example, the effect of dosage in an inoculation with very virulent milk from a tuberculous cow. One cubic centimeter of this milk injected into the peritoneal cavity produced in sixteen days, besides the local lesion of the peritoneum, tuberculosis of all the internal lymphatic glands, of the cervical glands, and of the liver and spleen, but not of the lungs; whereas one cubic centimeter of a 10 per cent dilution of the same milk produced in the same time a local lesion practically limited to the omentum, with tuberculosis of the spleen and of the mesenteric glands, but of no other parts. In another animal, however, in eighteen days a similar dose produced tuberculosis of the omentum and of the spleen, of the cœliac and anterior mediastinal glands, and to a slight extent of the liver. In these experiments, therefore, using the same virulent material, dilution of the milk produced in the same time a limitation of the disease. This feature is more evident in the results of experiments in inoculation of the meat of tuberculous animals. As I have said, with tuberculous material accidentally smeared over the meat during removal, very varying results were obtained; one portion of meat, for example, contained but a small amount of the virus, while another portion contained a larger amount. A guinea-pig, which had been inoculated with meat in each groin, died in sixty-two days, and at the seat of inoculation on one side a small scar was found, covered by a brown crust; this on examination showed the structure of a chronic tubercular lesion with tubercle bacilli. None of the internal organs or glands were affected, but there was a small sub-peritoneal abscess, opposite the spleen, which contained a few tubercle bacilli. This case illustrates in a marked manner the effect of inoculation of a small dose of the poison, inasmuch as in sixty-two days there was practically a local tuberculosis only; whereas if the material had been greater in amount, the disease would have spread in this time to all the glands and organs of the body. It is impossible not to see in this experiment a reproduction of some of the pathological features of local tuberculosis in man. Other experiments may be quoted; for example, a rabbit was inoculated with one cubic centimeter of meat juice in each groin: the animal was killed in 120 days, at a time when if the material had been virulent all the organs and glands of the body would have been affected; but the only lesion present was in the inguinal glands of one side, the lesion containing tubercle bacilli. In another rabbit inoculated with two cubic centimeters of meat juice in each groin, death occurred in sixty-six days, and a small tubercular caseous mass, containing numerous tubercle bacilli, was found in the right thigh. This experiment illustrates the same points as the two former; but another point also, inasmuch as the injection in the right thigh accidentally took place in the muscles of the limb, and the development of tubercle bacilli was more or less prevented by the muscular tissue. These are extreme cases of local tuberculosis resulting from the inoculation of meat. In many others it was likewise found that the degree of tuberculosis at the time of death was not so advanced as when larger doses of virulent tuberculous material were used.

Feeding Experiments.—Inoculation experiments, although instructive from the point of view of infection, do not reproduce the kind of cases that occur in the human being or in natural tuberculosis. Although inoculation-tuberculosis has occurred in the human being, the great majority of cases of the disease are to be ascribed to other modes of infection. Feeding is one of these. The results of feeding with tuberculous material will be discussed as they occur in guinea-pigs, pigs and calves; and, as in the inoculation experiments, with virulent and with non-virulent material.

If guinea-pigs be fed with one dose of virulent tubercular material obtained from the cow or man, the first lesion observed, as in other cases of infection by the disease, is a local one in the small intestine and cæcum. This is first apparent to the naked eye (and, indeed, to microscopical examination) at the end of from eighteen to twenty-one days. Previous to this no naked eye lesion is discoverable, either in the Peyer's patches or in the mucous membrane, nor does a careful microscopical examination of the mucous membrane show tubercle bacilli; however, no examination by means of sections can be extensive enough, within practical limits, to make sure of their absence. The frequency with which the small intestine or the cæcum is affected is variable. Of twenty animals rendered tuberculous by feeding, the disease was present in the small intestine in all but one, which had been fed with sputum; and the cæcum was affected in all but three. The frequency of the infection of the cæcum in the guinea-pig is explicable by the fact that it contains large and numerous Peyer's patches, and thus differs greatly from this organ in man and carnivora. From the intestines the disease spreads to the mesenteric and the cæcal glands in about twenty-eight days from the commencement of the experiment; from these it spreads to the cœliac glands, the liver, spleen, posterior mediastinal and bronchial glands, and to the lungs. In some animals, living a long time, the anterior mediastinal glands are affected; as are also the glands in the lesser omentum and the lumbar glands. As in inoculation experiments, the course of the disease is similar when virulent tubercular material is used; that is, a local lesion is produced from which infection takes place to the neighbouring lymphatic glands, and thence to the other glands and organs of the body in order.

In pigs fed with virulent tuberculous material the pathological course of the disease is practically the same as in guinea-pigs; namely, from a local lesion in the alimentary tract the infection spreads to the neighbouring lymphatic glands, and thence to the organs of the body. But in the pig the tonsil is one of the chief localities for the absorption of the tubercular virus. The following case may be taken as a typical example of advanced tuberculosis from feeding in the pig. There was a large tuberculous ulcer of the right tonsil, the corresponding lymphatic glands showing advanced tuberculosis, which had spread to the chain of cervical glands: there were numerous tubercular ulcers in the cæcum, and the cæcal and mesenteric glands were all affected by the disease: the glands in the lesser omentum, the cœliac glands, and the posterior mediastinal and bronchial glands, were also affected, and there was tuberculosis of the liver, spleen and lungs. The local lesions in this case, however—those, that is, which showed the way in which the virus had entered the body—were the right tonsil and the cæcum.

A healthy pig was fed once with 120 grammes of tuberculous lung from a cow. It was killed in fifty-seven days, and a small tubercular ulcer, ¾″ by ½″, was found in one of the Peyer's patches in the middle of the ileum; otherwise the alimentary tract was normal. Nearly all the mesenteric glands were tuberculous, as well as the posterior mediastinal and the glands in the lesser omentum; while the liver, spleen and lungs showed extensive miliary tuberculosis. This experiment is of importance, as showing that the local lesion from feeding may be out of all proportion to the tuberculosis present in the organs of the body; for, whereas only one small ulcer was present in the intestine, all the mesenteric glands were affected, and the tuberculosis was extensive in the important solid organs of the body. It will be seen that this case, the result of feeding with a large dose of the virus, lies between the one previously quoted and that of feeding with non-virulent tuberculous material.

In calves fed with virulent tuberculous material the local lesion is present in the small intestine, and less commonly in the cæcum. The mesenteric glands are always affected, and, when the cæcum is attacked, the cæcal glands. The disease then spreads to the posterior mediastinal and bronchial glands, and usually to the lungs. The cervical glands may be subsequently affected, as well as the retro-hepatic glands. Two points, however, must be noted: (1) That, as in the pig, the glands below the jaw may be affected, showing that the absorption of the virus has taken place through the pharynx; and (2) that tuberculosis of the pleura in the form of "grapes" may occur without the lungs being affected. This result is of some importance from the pathological point of view. The case occurred in one of four calves kept in the same shed, which received at one feeding from the same trough one kilogram of a mixture of tuberculous udder, lung, and lymphatic gland, finely minced. All the calves became tuberculous, and were killed at varying periods. One was killed in eighty-five days, and besides showing ulceration of the intestine and an infection of the cæcum and of the mesenteric and cæcal glands, it presented tubercle in the posterior mediastinal and bronchial glands, in the lungs, in the pleura (as "grapes"), and in the cervical glands. Another calf, which was killed in 259 days, showed tuberculosis of the small intestine and of the mesenteric glands, of the retro-hepatic glands, of those below the jaw, of the posterior mediastinal and bronchial glands; although the pleura was extensively diseased, in the form of "grapes," the lung was quite normal. It is important, therefore, to note from this experiment that when the animal was fed with tuberculous material the pleura may be affected even though the lung be quite healthy. The infection of the pleura to the exclusion of the lung probably took place in this case from the bronchial and the posterior mediastinal glands.

Most important results were obtained when animals were fed with non-virulent tuberculous material. As an illustrative example, an experiment may be quoted in which four guinea-pigs were fed in the course of two days with 200 cubic centimeters of tuberculous milk which was not very virulent. Each animal got about 50 cubic centimeters of the milk. One died after twenty-five days, and showed no tuberculous lesion; the other three died in forty-nine, fifty-three, and sixty-seven days respectively. In these three last tuberculosis was developed, but the disease was present only in the intestines and mesenteric glands in the first two, and only in the mesenteric glands in the third. All three animals, therefore, showed a limitation of the disease; if they had been fed with virulent tuberculous material the disease would have spread to all the glands and organs of the body during the time that they lived. The last animal showed a point which is of great importance in the study of the mode of infection of tuberculosis: there was no local lesion in the intestine, yet the disease was present in the mesenteric glands, and nowhere else in the body. The conclusion is clear, therefore, that the bacilli had passed through the intestinal wall, without producing the characteristic local lesion, and had stopped and grown in the mesenteric glands.

This point is well illustrated in the result of feeding pigs with non-virulent tuberculous material. In these cases there was no local lesion in any part of the gastro-intestinal tract, either in the fauces or in the small or large intestine. Tubercle is developed in the lymphatic glands in connection with the gastro-intestinal tract, and may extend to other glands and organs of the body. This occurs when pigs are fed with the meat from tuberculous cows, or with milk only slightly virulent from cows with tuberculosis of the udder. Thus, a healthy pig was fed with about 12 litres of milk from a tuberculous cow: it was killed in sixty-eight days, and tuberculosis of the mesenteric glands alone was found—an extensive examination of all the other glands and organs of the body showed the structures to be perfectly normal. That this was only slightly virulent milk was also shown by the experiments on guinea-pigs, which, however, need not be further referred to. The site of invasion of the tubercle bacilli in this animal was therefore through the small intestine, since the mesenteric glands were affected. The small intestine is not the only tract through which the tubercle bacilli may pass without producing a local lesion. Thus, one pig was fed with over 4½ kilograms of meat from a tuberculous cow, and was killed in sixty-seven days. Tuberculosis of the glands below the jaw on the right side was found, as well as of the lungs: there was no lesion in the tonsil or pharynx, and all the other organs of the body were normal. In this case the mode of invasion was through the right tonsil or the right side of the pharynx; and the disease, after affecting the lymphatic glands in connection with this part, extended to the lungs without affecting the cervical glands or the glands of the thorax. This was a very instructive case, inasmuch as it reproduced the distribution of the lesions in some cases of pulmonary tuberculosis in man, in which, following the development of "scrofulous glands" in the neck, disease of the lungs supervenes.

In another pig, which was fed with 4 kilograms of meat from a tuberculous cow and was killed in 106 days, there was tuberculosis of the glands below the jaw on the right side, of the cœliac glands, and of the liver and spleen. In this case, likewise, the mode of invasion was through the right tonsil or right side of the pharynx, but also through the upper part of the gastro-intestinal tract, for the cœliac glands were affected. The occurrence of tuberculosis in the liver and spleen possibly occurred by the infection from the cœliac glands passing backwards to those organs.

A fourth case of tuberculosis in a healthy pig followed the feeding with over a kilogram of meat from a tuberculous cow. The animal was killed in 203 days, and tuberculosis of the glands and the omentum, the cœliac, bronchial and posterior mediastinal glands, was found, as well as of one epididymis. In this case the mode of invasion was through the upper part of the gastro-intestinal tract, as the lymphatic glands in connection therewith were affected. The affection of the bronchial and posterior mediastinal glands is probably to be ascribed to infection from the abdominal glands affected, but the chief interest of the experiment rests on the fact that the epididymis, far removed from any connection by means of lymphatics with the glands affected, was tuberculous. In this case the disease is to be ascribed to infection carried by the blood-vessels.

The main features, therefore, of the results of feeding pigs with non-virulent tuberculous material are as follows:—

1. No local lesion is produced at the seat of invasion.
2. The lymphatic glands in connection with one or other part of the alimentary tract become affected by the disease.
3. From this focus quite distant parts may be affected, namely, the lungs, or even an organ so remote as the epididymis.

In the experiments on calves fed with either virulent or slightly virulent tuberculous material there was always a local lesion in the intestine when tuberculosis developed; but it is noteworthy that in both cases the local lesions in the intestines frequently did not proceed to ulceration, but consisted in small nodules in the Peyer's patches, which caseated, and frequently became calcareous. Calcification of these nodules might be found, even though there was active and spreading tuberculosis in various organs of the body. A similar observation was made in adult cows, the subject of natural tuberculosis; and the same thing occurs in the human being—the main fact is that the local lesion is out of all proportion to the tuberculosis which subsequently develops itself throughout the body. In calves sputum is not so highly infective a material as the tuberculous material from the organs of a cow. The course of the disease in the latter instance has already been described; and as regards sputum it may be stated that in one experiment two healthy calves were fed out of the same tub with 440 cubic centimeters of sputum from two cases of pulmonary tuberculosis, containing numerous tubercle bacilli. One calf was killed in fifty-six days, and thirteen nodules of tubercle were found scattered through the Peyer's patches of the small intestine; there was also tuberculosis of the mesenteric glands, but of no other glands or organs of the body. The second calf, which fed equally with the first, was killed in 138 days, and showed no tuberculosis, every organ and gland in the body being quite normal. This was a good illustration (of which many might be quoted) of animals exposed to the same degree of infection of tuberculosis—one developing the disease, the other not. In this particular instance the occurrence is explained by the fact that the calf that exhibited tuberculosis, being a Jersey, was more delicate than the other, a half-bred shorthorn.

Inhalation Experiments.—Numerous inhalation experiments have been performed (Villemin, Koch, and others), with the result of transmitting the disease to animals. The bacilli in pure cultivation have been sprayed on to the faces of animals, and a pulmonary tuberculosis has resulted; and tuberculous material has been dried and powdered, and allowed to be inhaled by the animals, with the almost certain result of producing pulmonary tuberculosis. This experiment, however, is dangerous for the workers, one of whom contracted a tuberculous and fatal broncho-pneumonia in this manner (Nocard).

Modes of Infection in Natural Tuberculosis in Animals.—In cows the mode of infection is either by means of the lungs or the intestines. In cases of tuberculosis in cattle the lungs and pleura are affected in about 40 per cent of the cases; the lungs alone, in 20 to 25 per cent; the pleura and peritoneum, in 15 to 20 per cent, and in the remaining cases the lymphatic glands, the genital organs, mammæ, bones, etc. (Nocard).

This, however, is not a valuable mode of classification, except to show that, as in man, the majority of cases of tuberculosis affect the lungs and thoracic organs. In the cow it must be remembered that the occurrence of "grapes" is an anatomical peculiarity of the disease, such bunchy tubercular vegetations not occurring in the pleura of man. The analysis of twelve cases of natural tuberculosis in the cow, in which every organ and gland of the body was examined, gave the following result:—The disease was primary in the lung in eight cases; primary in the intestines without affection of the lungs in one case; and in the intestine with affection of the lungs in three cases. The statement that these last three cases were primary in the intestine rests on the fact that the intestinal lesion, having calcified, was older than that in the lung. In cattle, therefore, the disease must be considered as most frequently an inhalation tuberculosis, and less frequently an ingestion tuberculosis. In the cow, when the lungs are affected, the posterior mediastinal glands are usually tuberculous; and, except in certain cases which occur in children, this constitutes an anatomical difference between pulmonary tuberculosis in the cow and in man. The disease, as it occurs in the cow, may thus be divided into two classes, namely, (1) where it is limited to the thoracic organs and glands, and (2) to the abdominal organs and glands. In cases of disease in the thorax it is highly probable, even if only one set of glands in the abdomen be affected, especially if this be the mesenteric glands, that the mode of invasion of the virus has been through the intestines; this is evident from the experiments on pigs which I have quoted. Thus, cases occur in which there is extensive tuberculosis of the lungs, of the bronchial and posterior mediastinal glands, of the glands in the lesser omentum, and of the liver. In such cases as these it is probable that the glands of the lesser omentum are those first affected; the disease spreads thence to the liver, to the posterior mediastinal glands and bronchial glands, and thence again to the lungs.

In the pig the disease is almost solely an ingestion tuberculosis, and has the features which have been described previously.

In the horse, infection occurs both through the intestines and through the lungs, most frequently, however, by the former mode; so that in most cases the abdominal organs are the chief ones affected, well-marked peritonitis being observed. This does not occur in the cow or the pig. The lung is usually affected secondarily.

Modes of Infection in Man.—In human tuberculosis, many as are the years during which it has been the subject of study, there is a great want of accurate information as regards the distribution of tuberculous lesions in a large number of cases; yet it is only by a consideration of large numbers that the modes of infection can be determined. The three modes of infection by which tuberculosis can occur after birth are by the inoculation, feeding, and inhalation of tuberculous material; to these may be added a fourth, as when infection is carried from the mother to the fœtus in utero.

Inoculation tuberculosis occurs in the human being accidentally, as in cases of wound of the hand during a post-mortem examination of a tuberculous subject. Some of the warts which appear in these cases (*verruca necrogenica*) are of a tuberculous nature. Death from pulmonary tuberculosis has also been known to follow inoculation of the finger after a longer or shorter interval. We may ask whether lupus is not in some cases a form of inoculation tuberculosis, following inoculation of the skin with tuberculous material not virulent in degree, as in the already quoted case of local tuberculosis of the skin occurring in a guinea-pig.

The more usual modes of infection in man, however, are by way of ingestion and of inhalation. Speaking generally, ingestion tuberculosis is a disease of childhood; inhalation tuberculosis a disease of young adult life, although it may occur at all ages. When the lungs alone are the seat of tuberculosis at death, as they so frequently are, and no old or recent tubercular lesion is found in or near any part of the alimentary tract, the mode of infection unquestionably was by inhalation of .tubercle bacilli. Similarly with the intestine; in cases where there is tubercular ulceration of the intestine, or even tubercular nodules in the intestine, with tuberculosis of the mesenteric glands or peritonitis, and no infiltration of the lungs, the mode of invasion has doubtless been by way of the mucous membrane of the intestine. But there are many cases which present great difficulties in their explanation—cases of so-called primary tuberculosis of the bones and joints, of the kidneys, of the epididymis, and of the brain or meninges. Post-mortem records of these have not been made with sufficient accuracy from the present point of view to permit us definitely to indicate the mode of infection in many of them. It must be remembered, firstly, that the local lesion which is developed at the seat of invasion may be out of all proportion to the subsequent tuberculosis; secondly, that from this local lesion a distant part of the body may be affected by the disease; and, thirdly, that the local lesion may heal and be found either as a fibro-caseous or calcareo-caseous nodule in the lung, or as a healed ulcer in the intestine, or as a calcified mesenteric gland without ulceration of the intestine. In some cases of primary tuberculosis in the parts mentioned old lesions are found, either in the lungs or intestines; for example, in cases of meningitis a few healed ulcers may be found, or a calcareous mesenteric gland; and in cases of tuberculosis of the epididymis, where fibroid and calcareous nodules are found in the lungs, there is no difficulty of explanation. But there are cases in which no local lesion, old or recent, can be found in the lungs, the intestines, or the neighbouring lymphatic glands. The explanation of such cases appears to be given by the results of the previously recorded experiments in animals, which have shown that the tubercle bacilli may enter the body without producing a lesion in the mucous membrane; and that even if one of the glands in connection with the gastro-intestinal tract become tuberculous, this may readily lead to disease of a distant part. It is quite possible in the tissues of children, in which absorption is active, that tubercle bacilli may pass even through lymphatic glands without producing a lesion; or more probably may enter the circulation from the mucous membrane and be carried to a distant part—such as the joints, bones, or the meninges—and so produce primary tuberculosis in those parts. In any case, whatever the exact path of infection, it is certain that the bacillus must pass through some portion either of the gastro-intestinal or of the respiratory tract.

Spread of the Disease in the Body after Infection.—Two classes of cases have to be considered, in one of which (and these are the majority) a local lesion is produced at the seat of infection; in the other there is no local lesion, but either a lymphatic gland in connection with the organs which usually constitute the path of the infection is affected, or, without infection of the lymphatic glands, a distant part may be affected by the tuberculosis primarily. When there is a local lesion in the early stages of the disease, a spread of infection takes place mainly by lymphatic channels, as I have fully explained in the account of experimental tuberculosis; but infection also occurs by actual contact of the tuberculous lesion with neighbouring parts, this being most evident in the lungs, and in cases in which the pleura infects the peritoneum after adhesion to the diaphragm. The third mode of spread of the disease is by means of the blood-vessels; this takes place when the blood-vessels are themselves infected by tuberculosis, as in the lungs they very commonly are; the tubercular lesion ruptures into the lumen of the vessel, and the virus is carried to distant parts. In this way the occurrence of tuberculosis of the liver and spleen in primary tuberculosis of the lungs is explained, the occurrence of meningitis likewise, and the infection of such distant parts as the joints and bones. I have referred to another mode of infection, namely, from mother to fœtus in utero. Instances of tuberculosis have been described in the fœtus when born, or in the early months of life, and are attributable to this cause. It is evident that this can only occur when there is tuberculosis of the placenta, for as there is no actual connection between the blood-vessels of the mother and those of the fœtus, the tubercle bacilli cannot be said to find their way through the walls of uninjured vessels.

Cases of primary tuberculosis in the bones, joints or epididymis—that is, in parts far removed from the ordinary channels of infection—may lead to a generalised tuberculosis; inasmuch as there is no direct lymphatic connection between the parts affected, the spread of the disease in these cases takes place presumably by means of the blood-vessels.

Sources of Infection.—The sources of infection in tuberculosis are deserving of the closest study, to enable us by prophylactic measures to diminish the mortality from the disease. In many minds great difficulties surround the opinion that tuberculosis can be discussed as an infective disease. These difficulties are relics of the past, during which the discussion of "phthisis" has been mainly limited to purely anatomical and clinical considerations. The question has often been obscured by such a term as "the communicability of phthisis," used as if "phthisis" were a disease which could be communicated from one person to another as rapidly as scarlet or other infecting fever.

Tuberculosis has all the characters of an infective disease. It has an incubation period; it is associated with fever, and certain other definite symptoms which will be discussed later. There can be little doubt that the long duration of cases of tuberculosis has been the great bar to the acceptance of the disease as an infective malady. If it had a short incubation period, and if, as in some infective fevers, death took place in a short time, there would be no doubt of the infectiveness of the disease. The word "phthisis" has also greatly obscured the subject; it is better to discard it and use the term "pulmonary tuberculosis" for the disease when it attacks the lungs—for "consumption," as it is usually called. Few of the cases called "phthisis" are not pulmonary tuberculosis; indeed this is to understate the matter, inasmuch as one of the surest means of diagnosing cases of "phthisis" is the discovery of tubercle bacilli in the sputum, and the diagnosis is sometimes made from this fact alone. There is, as a rule, no difference of opinion when tuberculosis attacks other parts of the body, and therefore the foregoing explanatory remarks in relation to "phthisis" are necessary. Tuberculosis is an infection; it is due, that is, to a virus which is introduced into the body; it cannot arise *de novo* in the body, and therefore, as has been stated, the sources of infection—that is, the material which in natural tuberculosis is introduced into the body and produces the disease—must be studied with great care. It has been stated that the bacillus is a parasite and not a saprophyte, that it has no independent existence outside the body. But there are numerous sources of infection by tubercular material from human beings or from animals the subjects of the disease. Thus, from human beings there is the sputum from the lungs in pulmonary tuberculosis; the urine or the fæces, when the urinary tract or intestines are affected with the disease. Milk from a tuberculous cow may be a source of infection, or meat from cow, pig or fowl; and tuberculous organs or parts removed from man or animals may also be sources of infection. By far the most important of all these, however, are sputum and milk.

1. *Sputum* in the moist state, when inoculated, inhaled, or used for feeding, produces a spreading tuberculosis, as has been frequently shown by experiment. In dried sputum the bacilli retain their vitality for a very long period, even for eight or twelve weeks; and in this form they can produce tuberculosis in animals by inhalation. Considering the number of tuberculous human beings in the world, and the absence of precaution in the treatment of the sputum, this is probably the most frequent cause of tuberculosis, and especially of tuberculosis of the lungs. The dangers from sputum arise not so much in the open air, as in the habitation or the room occupied by a patient. In the open air it is soon dried, and the bacilli are rapidly killed by means of the sunlight. In the room occupied by the consumptive, not only does the handkerchief, which frequently receives the expectoration, become highly infective, but also the clothes of the patient, the bedclothes, and the walls and furniture; soiled handkerchiefs may be laid on the mantelpiece or elsewhere, expectoration may fall upon the floor. Thus the room in which a consumptive has lived, especially towards the end of the disease when he is in bed and occupies one only, becomes highly infective if no precautions be taken to isolate or destroy the sputum; even when spitting-cups are used, these have been known to transmit tuberculosis by inoculation to the person who washes them, as by way of wounding a finger. Considering that sputum is a tenacious material, that it is readily collected in a vessel, and that its infectivity is readily destroyed, either by antiseptics (carbolic acid), or by heat, there can be no doubt that if proper precautions were taken in destroying this highly infective material some progress would be made—and perhaps a very great one—on the road to prevention of the disease. Many direct instances of infection by sputum have been recorded, some of which have occurred after inoculation. These were such cases as those just mentioned, of wounding the finger when cleansing the utensils containing sputum, or cases of tubercular prepuce and inguinal glands following circumcision performed according to the Jewish rite by a consumptive priest. Direct infection by sputum, causing pulmonary tuberculosis,

occurred from a midwife in advanced pulmonary tuberculosis, who was accustomed to blow down the mouths of newly-born children. No fewer than ten of these became tuberculous. To this category also belong those cases where a healthy husband contracts tuberculosis from a consumptive wife, or *vice versâ*.

2. *The milk* from cattle, the subjects of tuberculosis of the internal organs and of the udder, if consumed in the raw state, is another source of infection. When the udder is not diseased the milk is not infective, and never contains tubercle bacilli; although it must be remembered that tuberculosis of the udder may supervene at any time in a tuberculous cow. Experimentally this has been definitely proved. With the milk of eight cows, the subjects of tuberculosis in varying degrees from a very slight amount of disease to advanced and generalised tuberculosis, but without disease of the udder, twenty-six animals (rodents) were inoculated, and forty-one animals (guinea-pigs, pigs and rabbits) were fed; none developed tuberculosis. On the other hand, when the udder is diseased the milk usually contains tubercle bacilli, which are discoverable on a microscopical examination. If the disease, however, be not far advanced it may be difficult or impossible, within practical limits, to discover tubercle bacilli, although these, as shown by the results of inoculation and feeding, are present. Thus, to quote the experimental results: with the milk of five tuberculous cows, the subject of tuberculosis of the internal organs, varying in degree, and with varying degrees of tuberculosis of the udder, twenty-one animals were inoculated—all developed tuberculosis; twenty-seven animals were fed—nineteen developed the disease. The milk given by such cows, therefore, was very virulent, and must be considered as the chief mode by which an ingestion tuberculosis occurs in man. The butter made from such milk (even when diluted with normal milk), the buttermilk and skim-milk are also highly infective, and give tuberculosis both by inoculation and by feeding.

Milk is a source of infection chiefly in children, in whom until the eighth year of life it ought to form the chief article of diet; to the ingestion of milk is no doubt to be ascribed practically all the cases of intestinal tuberculosis and of tubercular peritonitis that occur in children. In some instances it has been directly shown that milk is a source of infection in childhood (Demme), producing intestinal tuberculosis. It must be granted, from the experiments in pigs which have been recorded, that it may also be a source of tuberculous (scrofulous) glands in the neck. The sputum, or any tuberculous material that gets into the mouth, may of course affect these glands also. Some cases, where tuberculosis has affected the socket of a lost tooth, are possibly ascribable to milk. The danger is no doubt diminished from the fact that in most of the milk distributed in large towns the milk of all the cows of the herd is mixed, producing a more uniform quality. But this is not always so; the milk of a single cow is frequently used for feeding children; and even when the milk is mixed with non-tuberculous milk it is quite possible for one individual to get a sufficient dose of the virus to produce tuberculosis. Infection by milk is prevented by boiling it for at least a minute. As soon as tuberculous cattle are rigidly excluded from the dairy there is no doubt that there will be a great diminution in cases of abdominal tuberculosis in children.

3. *The meat* removed from tuberculous cattle is infective in a varying and somewhat irregular manner. Experiment has shown that the infection depends, not on tuberculous lesions which are present in the muscular tissue itself, but on the contamination of the meat during its removal from the carcase; either by the meat touching a tuberculous part, or by infection from a knife or cloth used by the butcher which has previously incised or wiped a tuberculous part. Besides this superficial contamination, tuberculous glands, either the lumbar or popliteal glands, are not infrequently left in the carcase when sold, and these might in some instances be imperfectly cooked, and, containing living bacilli, would when swallowed be a source of danger. Tuberculous lesions of the muscular tissue itself are extremely rare, and do not account for the tuberculosis which results from the inoculation or feeding of animals with the meat. The experimental results to test the infectivity of meat may be quoted. Meat from twenty-one cows, which were in varying stages of tuberculosis from mild to advanced, was inoculated into forty-eight animals; of these, ten developed tuberculosis: 102 animals (guinea-pigs and pigs) were fed on it, and six developed tuberculosis. It is thus seen that raw meat is a much less infective material than raw milk. The danger of meat in the production of tuberculosis is diminished by cooking, since by any mode of cooking—whether roasting, broiling or boiling—the surface of the meat is raised to a temperature which is fatal to the tubercle bacilli contained in the tuberculous material contaminating it. Medicinally, raw meat is sometimes given, and unless precautions be taken this may be a source of tuberculosis. The more advanced the tuberculosis of the cow, the more likely is the meat to be infective; therefore, no meat ought to be passed for consumption from a cow in which the anatomical distribution of the disease shows that it has become generalised.

4. *Tuberculous organs or tuberculous parts* removed by operation, as well as the normal excreta from organs which are the seat of the disease, may be sources of infection in tuberculosis. Organs from the slaughter-house given to animals may produce tuberculosis in them, and all tuberculous parts when dried may, like the sputum, be sources of infection. All such parts ought either to be destroyed by heat, as in the case of solid organs and parts, or rendered sterile by antiseptics, as in the case of urine and fæces; these precautions would prevent at least some of the cases of tuberculosis in animals, and possibly in man also.

Preventive Measures.—It is evident from what has been said of the sources of infection that they are all preventible. As regards the milk and the meat, public regulations for limiting the supply of milk to that from healthy cows alone, and for preventing the sale of meat from cattle in an advanced stage of tuberculosis, are necessary; and would, no doubt, in time remove meat and milk from the list of sources of tubercular infection. Public regulations, however, develop slowly, and not infrequently are imperfectly carried out; but as regards milk, tuberculous infection is so readily destroyed by boiling that this ought to be done as a precautionary measure by every householder. Similarly with the meat from tuberculous cattle; to sterilise the surface would, in the majority of instances, be sufficient to destroy the infectivity of the material. The destruction of tuberculous organs removed in the slaughter-house ought to be compulsory, and such organs ought not to be used in any way whatever. The destruction of parts removed by an operation is usually effectively performed; when preserved in alcohol the tubercle bacilli are killed, and when not preserved the parts are usually burnt. The urine can only be a source of infection in tuberculosis in rare instances; but it is evident (inasmuch as intestinal tuberculosis with diarrhœa is so common an infection both in man and animals) that the fæces, after drying in the stall, or after contaminating the bed-pan, may frequently be a source of infection. In the case of human beings the use of antiseptics, such as carbolic acid or hydrochloric acid, is sufficient to destroy the infection; and cattle, when they come to the stage of an exhausting diarrhœa due to intestinal tuberculosis, ought to be slaughtered and the stalls disinfected. Lastly, the sputum is a preventible source of infection. No State regulations will make people careful in the disposal of tuberculous sputum; but as soon as consumptive individuals are educated to understand that the sputum which they bring up from the lungs is a source of danger not only to those surrounding them, but to themselves, and that the danger is to be obviated by a very little care, precautionary measures will, no doubt, be taken by these persons, and in this way the most common cause of pulmonary tuberculosis will be prevented.

Tuberculosis is not a disease in which the infective agent, the tubercle bacillus, is so widely distributed that no precautionary measures are available against its spread and its invasion. The bacillus is not a saprophyte. It exists only in tuberculous lesions and in the products of their degeneration; thus in the human being tuberculous infection tends to become limited to places inhabited by consumptives; and in cattle it is a disease of the stall.

Immunity is either natural or acquired. In tuberculosis, under certain conditions, there is a local immunity of some tissues and organs which prevents their invasion by the disease. There is a natural immunity both in some men and in some animals, but no animal has as yet been rendered immune to the disease; that is, there is no means by which immunity can be conferred on any animal or on man.

Local Immunity of Tissues.—This has already been indicated in discussing the parts most frequently affected by tuberculosis, but there are certain parts so rarely affected by the disease that they may be considered naturally immune. When tuberculosis affects man or animals it is a local disease, in so far that, however many parts may be affected, only those parts that contain the lesions are infective, and each infected part has, so to speak, a separate existence and course of its own. Parts of the human being which are immune to tuberculosis are the mucous membranes of the mouth, pharynx, œsophagus, stomach, and first part of the duodenum. Not that tuberculosis has never been observed in these parts, but it occurs very rarely, and only in advanced cases of the disease. The absence of infection of the pharynx and œsophagus in tuberculosis is to be explained by the rapid passage of the infective material through them in swallowing, the mucous membrane being, moreover, protected by stratified epithelium. In the stomach and first part of the duodenum, however, the great hindrance to the development of tuberculosis is the hydrochloric acid which is secreted in the gastric juice. This prevents the development of the tubercle bacillus, and may even be fatal to it. Muscular tissue is rarely affected by tuberculosis, and this, again, is perhaps to be ascribed to the acid which is formed by the muscles during their contraction; in an acid medium the tubercle bacillus cannot grow. Tuberculosis of muscle, however, does occur, but only in advanced cases of the disease, and chiefly in animals. Reference has already been made to the relative immunity of the kidneys in cases of experimental tuberculosis in guinea-pigs. In rabbits, on the other hand, the kidneys are frequently affected in generalised tuberculosis, and they are affected in cattle, pigs, and other animals, as well as in human beings.

Immunity to natural tuberculosis is only a relative term; it does not mean that the disease cannot be conveyed to animals by inoculation or feeding. Animals differ in the degree to which they naturally show the disease, and in the resistance which they exhibit against the inoculation of tuberculous material. Tuberculosis is a natural disease in man, cattle, pigs and birds in a state of domesticity. It is rare in sheep, goats, horses, dogs and cats. It is a disease, therefore, of man who lives in houses, and of cows which are kept in stalls. There is little doubt that some human beings are naturally immune to tuberculosis, but this is a statement which it is impossible to prove. In cattle the disease is very frequent in certain places. From 10 to 20 per cent of all cows show tuberculosis. The degree of prevalence varies in different parts, and varies to some extent according to the breed of the cow. From statistics obtained from Copenhagen, 17·7 per cent of slaughtered oxen and cows were tuberculous, and 0·2 of calves; and in the Berlin slaughter-houses 15·1 per cent of oxen and cows, and 0·06 of calves. Pigs come far behind cattle in their susceptibility to natural tuberculosis. Out of 336,972 pigs slaughtered in Saxony in 1891 (a country in which bovine tuberculosis is very frequent) only 0·28 per cent were tuberculous. In Copenhagen, however, the percentage of tuberculous swine was 15·8 in 1890-3, and in Berlin 1·55 in 1892-3.

In Saxony, out of 85,701 sheep slaughtered in 1891, 30 were tuberculous, or 0·035 per cent. In Copenhagen the percentage (1890-3) was 0·0003, and in Berlin (1892-3) 0·0003. Goats and horses very rarely contract tuberculosis, and dogs and cats still more rarely. From the results of experimental tuberculosis in these animals it may be said that they are all capable of infection by inoculation with tuberculous material. Cattle are as susceptible to the disease as pigs, and it may be given to goats. The domestic carnivora—dogs and cats—vary somewhat in this respect. An adult dog will resist the subcutaneous injection of an amount of tubercular material which would produce generalised tuberculosis in a rodent or in a cow; no local lesion is produced in the dog, which retains its health. On the other hand, tuberculosis can be transmitted to dogs by the intra-venous or intra-peritoneal injection of a large quantity of bacilli. Similar remarks apply to adult cats; but kittens, on the other hand, are readily infected by the disease, either by inoculation or by feeding with tuberculous material. Of all the domestic animals, therefore, carnivora show the greatest resistance to the development of tuberculosis experimentally. A still greater immunity is possessed by the Algerian rat, already referred to. This animal, although it does develop tuberculosis after inoculation, lives for seven or eight months; and when killed and examined, well-marked retrogressive changes are found in the tubercular lesions. The resistance exhibited by fowls against the inoculation of human tuberculous material has been pointed out. It is also difficult to produce a generalised tuberculosis in guinea-pigs by avian tuberculous material, although this difficulty does not exist in rabbits. It is evident from what has been said that the question of immunity is as difficult of explanation in tuberculosis as it is in any other disease. In the present state of knowledge but little can be said of the factors which constitute resistance to the invasion of an infective agent—whether, on the one hand, this resistance resides solely in the formed elements of the body, or, on the other hand, in the liquids of the body, or in both. It is not known in what way resistance to tuberculosis may be increased, except in the vague sense of increasing the general health of the body.

But in the human being there are undoubtedly many conditions which diminish resistance to the invasion of tuberculosis, and these may now be considered. The effect of alcohol on the body must be one of these, since in those suffering from the abuse of alcohol tuberculosis is not an uncommon disease, and runs a rapid course. Syphilis is another disease which diminishes the resistance to tuberculosis; and also diabetes, in which disease the development of tuberculosis is not uncommonly the cause of death. In cancer, of whatever part, a tuberculous lesion in the lungs is very common. Obsolescent or retrograde tubercle in the lungs occurs in about nine per cent of all necropsies, and of these cancer occurs in by far the largest proportion. In Dr. Fowler's statistics they form about two-fifths of the cases, and in my own about two-sevenths. These statistics were obtained from the Middlesex Hospital, where a large number of cases of cancer die every year. In Heitler's statistics, obtained from the Pathological Institute of Vienna, the proportion of cases of obsolete tubercle found in cancer was one-seventh of all cases examined post-mortem. In cancer pulmonary tuberculosis is rarely found in an active state, but is almost always retrograde; and considering the frequency with which it is found, it may be said that, although the condition induced by cancer tends to the invasion of the body by the tubercle bacillus, it is inimical to the spread of the disease.

Conditions of diminished resistance to the disease are also observed in individuals who may be said to be generally non-resistant to infective disease; those, for example, whose bodily health is diminished by worry and excessive work, insufficient exercise, life in a close atmosphere, irregular or insufficient food; those who inherit from their ancestors a certain weak condition of body, and those who are readily affected by changes of temperature or by changes in mode of life.

There can be little doubt that previous injury to a part is in some cases favourable to the invasion of the tubercle bacillus; but the kind of injury is difficult to specify. In the case of pulmonary tuberculosis the disease not infrequently appears after measles and whooping-cough, in both of which catarrh of one or other part of the respiratory tract takes place. Similarly, the inhalation of certain kinds of dust (vegetable, animal or mineral), by inflicting an injury on the lung, may be considered to dispose to pulmonary tuberculosis. But this agency, again, is extremely difficult to determine, inasmuch as if dust be inhaled, as it usually is, in the company of fellow-workpeople, and not uncommonly in a close atmosphere, it is just as possible that the inhalation of dust is not simply the taking in metallic or other particles, but also dried sputum which has come from a consumptive fellow-worker; so that the question would not be one of previous injury to the organ affected, but one of direct infection.

The etiology of tuberculosis is centred round the bacillus tuberculosis; where this does not enter the body no tuberculosis can be manifested, and the other diseases, which have just been considered, only dispose to the reception and implantation of the micro-organism from the environment.

Although tuberculosis is most frequent between the ages of fifteen and twenty-five years, it may occur at any *period of life*. In rare instances it may be congenital; passed on, that is, from the mother to the fœtus when the mother is tuberculous and the placenta is affected. In childhood and adult life the disease is always an infection still, but influenced in some cases by an inherited condition of body. How far *heredity* conspires in the production of tuberculosis it is impossible to say. Several members of a family, the offspring of tuberculous parents, may exhibit the disease, but this is no strong argument in favour of the inheritance of what has been called the "tubercular diathesis"; if members of a family live together and die off successively, the family is constantly surrounded by infective material, the danger of which is unappreciated: it may well be, then, that many cases of so-called heredity are only cases of infective surroundings. In determining the question of heredity, not only must inherited defects in the structure of the thoracic walls, of the lungs themselves, and of the heart be taken into account, but also the mode of life, and the influence of surroundings on the individual.

Tuberculosis is a disease which affects the *sexes* equally. The consequence of tuberculosis in married persons, one of whom may come of a tuberculous and the other of a healthy stock while both become consumptive, has already been mentioned. Here again the carelessness in the disposal of the infective material (that is, the sputum), which is due to ignorance, no doubt plays the greatest part. *Pregnancy*, in some instances, delays the progress of the disease, which, however, often increases rapidly after confinement, owing to the lactation being beyond the powers of the patient. *Climate* and conditions of *soil* have but little influence on the development of tuberculosis, although drainage has been shown to have an influence on the mortality from the disease (Buchanan).

Pathological Diagnosis.—The pathological diagnosis of tuberculosis depends partly on the structure of the tuberculous lesion, and partly on the distribution of the lesions in the person or animal affected. As regards the anatomy, there is, with the exception of the presence of the bacillus, no element in the structure of the tuberculous lesion which is diagnostic of the disease. Thus the presence or absence of the epithelioid cells is not a characteristic of tubercle, nor is the presence of giant cells. Epithelioid cells may be absent from a tuberculous lesion; and giant cells, although more numerous in tubercle than in other lesions, are found normally as osteoclasts in bone which is being absorbed, and also in some forms of sarcoma. Necrosis of the central part is not characteristic of the tuberculous lesion, as this may occur in cases where a mucous membrane or an organ is invaded by other forms of cocci and bacilli. This bacterial necrosis is frequently observed in animals, and has been observed in man: it is characterised by the presence of whitish or whitish yellow nodules in the part affected, which nodules (microscopically) consist of a round-celled infiltration—a leucocytic infiltration, that is—which undergoes necrosis in the central part in practically the same manner as in tuberculosis. That which is distinctive of a tuberculous lesion, and distinguishes tubercular necrosis from other forms of bacterial necrosis, is the presence of the bacillus tuberculosis; if the tissue be stained in the manner directed and the bacillus found, the lesion is tubercular. A mixed infection may occur; that is, there may be a tubercular infection producing its characteristic lesion, and, in addition, an infection by other forms of bacteria—for example, a streptococcus; in this case both the bacillus tuberculosis and the other forms of bacteria are found in the necrosed tissue and among the leucocytes surrounding it.

The second point by which tuberculosis may be diagnosed is the distribution of the lesions. Although the distribution varies in individual cases, as the tuberculosis is localised or becoming generalised, yet in every case there is evidence of infection. For example, taking the local tuberculosis of the lungs as it occurs in man, there is the older lesion at the apex of the lung, and, spreading from this towards the base of the lung, there are numerous recent lesions in the form of the granulations which are diagnostic of the disease. Again, in ulceration of the intestine, it is not so much that the ulcers are transverse and occur in the lower part of the ileum, but that miliary tubercles are discovered in the base of the ulcer or beneath the peritoneal coat which establishes the diagnosis. And so with the other forms of local tuberculosis.

When the disease becomes generalised the distribution of the lesions is, as has been said, divisible into two classes. In the first class there is a local lesion at the seat of invasion of the micro-organism, and from this infection of the body occurs: in the second there is no local lesion at the seat of invasion. The neighbouring lymphatic glands may or may not be affected, and an irregular distribution of tuberculous lesions results. Examples of the first class have been given already, but may be mentioned again: cases, for example, where there are primary tuberculosis of the lungs and secondary tuberculosis of the liver or spleen, or meninges; or where there are primary tuberculosis of the intestines and secondary tuberculosis of the peritoneum, of the lungs, or other organs. The second class is, as has been seen, very large: it contains scrofulous glands of the neck, which may extend downwards and infect the lungs and other parts of the body; as well as tuberculous peritonitis without intestinal ulceration, but with subsequent infection of other organs; and, lastly, cases where the mode of invasion cannot be traced, as in primary tubercular meningitis, and tuberculosis of the bones and joints, from which subsequent infection of the body occurs. The mode of spread is, I repeat, of great importance, whether it be effected by mere contact, by means of the lymphatic system, or by means of the circulation of the blood to distant parts.

In some of its aspects, therefore, the spread of tuberculosis in the body resembles that of cancer, inasmuch as the chief modes are either by actual contact or by means of the lymphatic system. Both may be localised, and both may be more or less generalised.

Symptoms of Tuberculosis.—It is difficult to describe the symptoms of tuberculosis as a disease, inasmuch as they are complicated, and frequently obscured, by the special symptoms which arise when tuberculosis affects an important part. In common with other infective disorders it is a febrile disease, and it is known from experiment that it has a period of incubation. This is not observable in man, inasmuch as the lesions of tuberculosis, giving rise to few symptoms and physical signs in the early stages, are not discoverable till some time after they are formed.

As regards symptoms, tuberculosis may be described as a chronic febrile disorder, associated with wasting and frequently leading to death. The fever varies greatly. In rapid and advancing cases it may be high and continuous for a long period. In cases which advance less rapidly it may be a typical hectic fever, with an evening rise and morning fall. All variations between hectic and continuous fever are observed. In more chronic cases (and these are the most important, owing to the difficulty in their diagnosis) as well as in the early stages of cases where there is great resistance to the invasion of the disease, the fever becomes irregular. There is at no time high fever, and there may be periods of complete remission from the fever; but its long continuance leads to the suspicion of tubercle. Tuberculosis in this respect forms a marked contrast to cancer.

The fever is associated with wasting, which is frequently out of all proportion to the degree of it; and is most pronounced in cases where an important organ, such as the lungs, is affected, or where—as in tubercular peritonitis and tabes mesenterica—the absorption of food is interfered with.

The fever in all forms of tuberculosis is frequently accompanied by night sweats—the sweating occurring in the early morning, at the time when the temperature begins to fall. The sweating at night also is usually out of all proportion to the degree of fever, and is then due to the general condition of the patient.

Besides these symptoms, tuberculosis tends to produce anæmia, and also exercises a profound effect on other organs of the body. Fatty degeneration of the heart, liver and kidneys is observed in advanced cases. Lardaceous degeneration of the stomach, liver, spleen, kidneys and intestines, and gastric catarrh, with functional disorders of intestinal digestion, may also be present.

The special symptoms of tuberculosis are those relating to the parts locally affected by the disease. Thus, in disease of the lungs there is cough, with or without expectoration, and hæmoptysis; in that of the intestines there is diarrhœa, frequently with the passage of blood, and in that of the peritoneum there may be somewhat similar symptoms; in that of the bones and joints there is frequently pain, with or without the development of abscesses; in that of the epididymis there are frequently but few symptoms. In disease of the kidney pain and pyuria or hæmaturia may be present, and in that of the meninges the symptoms are those occurring in disease of the brain. Into the physical signs of the different forms of local tuberculosis and their special symptoms it is not necessary here to enter, as they are fully treated of elsewhere; but it may be remarked that the severity of the general symptoms of the disease depends upon the chronicity or acuteness of the spreading tuberculosis: with very chronic lesions there are but few general symptoms, which is explicable by the fact that the great fibrosis of the chronic lesion shuts it in, preventing absorption of the products which produce the general symptoms. In the acute lesion, on the other hand, the products, being rapidly absorbed, produce severe general symptoms. Other factors necessarily play a part in producing the severity of the symptoms, namely, the general condition of the patient and the presence of disease elsewhere in the body.

Acute general tuberculosis, or acute typhoid tuberculosis as it is sometimes called, is best termed acute generalised tuberculosis. As I have fully explained in discussing the pathology of the disease, it may occur in two chief forms, in one of which there is a generalised tuberculosis of the body directly following infection; in the other, after the persistence of a chronic lesion for some time, a generalised tuberculosis proceeds from it. Clinically the two classes of cases are very similar, and the nature of the latter event may not be understood until on post-mortem examination a chronic lesion of the lungs or intestine, too small to have given rise to physical signs, is revealed. The symptoms of acute generalised tuberculosis are those which have just been discussed, but they are accentuated. Thus the illness may begin acutely, and progress with high fever, night sweats, great emaciation, and bodily prostration, until the patient sinks into the typhoid condition which precedes death. The clinical feature of acute generalised tuberculosis is that with these severe symptoms there are but few signs of the local affection of organs. Thus, although the lungs may be found studded with tubercle after death, the cough is but little, or dry and hacking only, and without hæmoptysis: there is no pus in the urine (unless the kidneys were previously affected with chronic tuberculosis); there is no diarrhœa ascribable to the disease, inasmuch as any looseness commonly occurs towards the end of the illness, and is part of the typhoid condition. The heart presents no abnormal sign, but enlargement of the spleen may be discovered. The splenic enlargement in acute tuberculosis is never great, and does not often form the characteristic tumour in the left hypochondrium. Cerebral symptoms may supervene, perhaps early in the disease: headache and slight delirium with crying out,—symptoms not definitely characteristic of tubercular meningitis unless combined with retraction of the head, slowing of the pulse, ocular palsy (seen either in the pupils or as slight strabismus), or with the presence of tubercles in the choroid, when tuberculosis of the pia mater becomes evident. Acute generalised tuberculosis is always fatal, and ends in from six to twelve weeks.

Diagnosis.—Tuberculosis must be distinguished from other chronic febrile disorders associated with wasting. The difficulty in the diagnosis of tuberculosis rests on the fact that it may be present in the body for some time without definite physical signs of local disease.

1. *Typhoid Fever.*—In cases where at the onset of the tuberculosis the fever is high, and associated with great bodily depression and with wasting, the diagnosis from typhoid fever may have to be made. Physical signs of local tuberculosis may be absent, and the diagnosis rest on the following points:—First, in cases of typhoid fever there may be a history of infection, or of occurrences of the disease in the house or neighbourhood of the patient. Secondly, in typhoid fever diarrhœa may be frequent, and the appearance of the motions characteristic. Thirdly, the abdomen may present the characteristic swelling and gurgling in the right iliac fossa, as well as enlargement of the spleen. Fourthly, the appearance of the characteristic rose rash in successive crops may

be distinctive. It must be remembered, however, that there may be no history of infection in typhoid fever; diarrhœa may be absent throughout the whole course of the disease, and, although the typical signs of the abdomen are generally present, the rash may be very slight and not characteristic. In such cases an absolute diagnosis from tuberculosis may be difficult even for some days. Improvement of the patient, with a fall of temperature in the fourth or fifth week, is significant of typhoid fever, and against the presence of tuberculosis. In all these cases the signs of a local tuberculosis must be carefully sought for, inasmuch as if once the patient have been infected by tuberculosis, even though the local lesion produced is apparently healed, general tuberculosis may result, producing the symptoms above described. In these cases, therefore, the presence of the scars of scrofulous glands in the neck, of a healed lesion at one or other apex of a lung, of tuberculous joint disease, or of tubercular epididymitis, is suggestive of tuberculosis.

2. *Lymphadenoma and Leukæmia* may be febrile at some part of their course; and sometimes the fever in the early stages lasts a considerable time, rendering the diagnosis somewhat difficult. The diagnosis from tuberculosis rests on the fact that in lymphadenoma the superficial lymphatic glands are enlarged. This may occur in tuberculosis also, but in lymphadenoma all the superficial glands tend to become enlarged, while in tuberculosis it is chiefly the glands of the neck; also, in the latter disease, the glands tend to become adherent to the skin, and to produce ulceration and scarring, or they may diminish in size. In some cases of lymphadenoma, as in leukæmia, there is at first no enlargement of the lymphatic glands; the liver and spleen may, however, be enlarged, and in leukæmia the increase in the number of white corpuscles of the blood will settle the diagnosis.

3. *Syphilis.*—Syphilis in its active stage may produce fever, but as a rule there is but little difficulty in the diagnosis. Even in the absence of the history of a primary sore, there is usually the characteristic polymorphous rash, ulceration of the throat, falling off of the hair, and perhaps condylomas at one or other of the orifices of the body.

4. Collections of pus, or its absorption from some latent ulcerated surface, as of the nasal passages, may lead to febrile disturbances which, in the absence of discoverable physical signs, give rise to the suspicion of tuberculosis. This occurs, for example, in otitis media; not usually in the early stages, where the pain is characteristic and the membrane of the tympanum unruptured, but in old cases where chronic fever may be produced, either by granulations in the external auditory meatus blocking the escape of purulent discharge, or where there is chronic caries of the bones surrounding the internal ear, with or without meningitis. Indeed the question of tuberculosis has to be considered in many other cases, where fever is not explained by any discoverable local signs; such, for example, as in the formation of internal abscesses from whatever cause. Although some such cases are tubercular, the diagnosis will appear on the development of the abscess.

5. *Infective (malignant) Endocarditis.*—In certain cases diagnosis between acute generalised tuberculosis and infective endocarditis may be difficult. If in such a patient a chronic tubercular lesion be known, the symptoms (fever, wasting, and prostration) may be ascribed to a generalisation of the disease. But it is when no such local tuberculous lesion is evident that these difficulties arise, inasmuch as infective endocarditis is a disease of many aspects: it consists in an acute affection of the heart with multiple embolism and with enlargement of the spleen; and thus, if one or more cardiac murmurs be present, and especially if one or more of these vary in character from day to day, or again, if there be a persistent or loud pulmonary murmur, or if there be evidence of embolism, such as a sudden hemiplegia, a thrombosis of arteries of a limb, hæmoptysis (due to infarction of the lung), hæmaturia (due to infarction of the kidney), or severe pain in the left hypochondrium, with more or less sudden enlargement of the spleen, the case may be clear from the first as one of infective endocarditis. Yet at one period of infective endocarditis cardiac murmurs and the signs of embolism may be absent, and no diagnosis may be possible until the occurrence of embolisms on the one hand, or of local lesions characteristic of tuberculosis (such as meningitis) on the other, dispel our doubts.

Prognosis.—The prognosis of tuberculosis depends on whether the disease becomes localised or generalised. In the majority of instances the great danger of tuberculosis is the dissemination of the disease into important organs of the body; but this fear must be qualified by a consideration of the locality in which the primary tuberculosis occurs. Thus, in scrofulous glands of the neck the prognosis is as a rule good. The disease sometimes spontaneously heals; in other cases operative procedure leads to a cure. In some of these cases, however, the disease spreads down the glands of the neck and affects the lungs. All such cases are of serious import. In primary tuberculosis of the intestines, with or without infection of the peritoneum, the disease sometimes becomes localised and heals. This occurs not infrequently in children. In many cases of primary tubercular peritonitis, where there is not extensive ulceration of the intestine, the disease remains localised, owing chiefly to the fact that, the progress of the lesion being slow, a large amount of fibrosis occurs, which blocks up the lymphatics leading from the peritoneal cavity, and so prevents the absorption of the virus, and thus the dissemination of the disease. On the other hand, from the intestine the disease may spread to the lungs and other parts of the body; all such cases are very serious.

Primary tuberculosis of the lungs is serious according to the extent of the local lesion: in the majority of instances general infection does not occur until the later stages. Prognosis depends, then, on the disease of other organs; as, for example, when there is fatty degeneration of the liver and kidneys, or lardaceous degeneration of the organs, or severe gastric catarrh. All such cases are grave. Tuberculosis of the kidney leads to complete destruction of a vital organ; and although usually more advanced in one kidney than in the other, both are not uncommonly affected. Tuberculosis of bones, of joints, and of the epididymis, when existing alone, is serious according to the results of surgical treatment, according to the signs of the dissemination of the disease, and the presence of the various forms of secondary degeneration of other organs. The symptoms and signs of general tuberculosis, occurring in any form of local tuberculosis, are always perilous, and usually end rapidly in death.

Treatment.—There is no specific treatment for tuberculosis. Nothing has yet been discovered to counteract the invasion of the tissues by the bacillus tuberculosis. The treatment, therefore, is either general, as adapted to the chronic febrile condition of the patient and to the defects in nutrition produced by the disease; or local, to the relief of special symptoms of tuberculosis in a particular part. This local treatment may be medicinal or surgical, and is discussed in other parts of this work.

SIDNEY MARTIN.

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S. M.

LEPROSY[1]

DERIVATION.—*Λεπρός*, scaly.

SYNONYMS.—English: *Elephantiasis Græcorum*, *Lepra*, *Satyriasis*, "Great Disease," "Mycle Ail"; and in the West Indies, "Joint Evil," *Cocobay*, "Bumpy Sick," and "Scrophula." French: *La lèpre*, *Ladrerie.* German: *Aussatz*, *Lepra.* Italian: *Lebbra*, *lepra.* Spanish: *Mal de San Lazaro*, *Lepra.* Norwegian: *Spedalske*, *Spedalskhed*, *Likpra.* Swedish: *Spetälskan.* Finnish: *Spetälskan.* Russian: *Prokaza*, *Crimka*, *Opasnaya*, *Kilka*, *Prypadek*, Crimean disease. Greek: *Elephantiasis*, *Elephas*, *Elephantos*, *Satyria*, *Satyriasis*, *Leontia*, *Leontiasis*, *Nousos Phoinike.* Sanskrit: *Kushta.* Arab: *Baras*, *Dsjudam*, *Jasam*, *Da el ased.* Indian: *Sunbahiri*, *Korh*, *Maha-korh*, *Rakt-*

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[1] In the preparation of this article, entrusted in the first instance to Dr. Rake, I have drawn largely from the published papers and reports of my late friend, and from some rough pencil notes which were found after his death. It contains, therefore, a summary of his extensive knowledge of the disease. Our views were in accord on most points; but I am inclined to lay greater stress on the personal communicability of leprosy as an ætiological factor, and I am unable to follow him in the nomenclature to which he still adhered.—P. S. A., Jan. 1895.

korh, *Pes*, *Charak*, *Ructa Kusta*, *Koostum coostaragum*, *Kod*, *Patgurme*, *Raght-pite*. Chinese: *Ma Fung*, *Ta ma fong*, *Li fong*. Japanese: *Shinshi*. Maori: *Ngerengere*, *Puhipuhi*, *Tuwhenua*. Icelandic: *Holdsveiki*.

Short Description.—A bacillary disease, apparently peculiar to man, of slow incubation and chronic course; manifesting itself in most cases by cutaneous pigmentary changes, and always by the formation of characteristic neoplasms, particularly in the skin, mucous membranes, and nerves, which give rise on the one hand to obvious thickenings and nodosities, on the other to alterations in sensation (analgesia, anæsthesia), and to tissue degenerations, ulcerations and progressive contractions and mutilations of the extremities.

History.—*Leprosy in Ancient Times.*—There is reason to believe that leprosy was a known disease many centuries before our era. The earliest reference to it appears to be in a papyrus discovered at Memphis—the "Ebers papyrus"—which was written during the reign of Rameses II., 1348-1281 B.C. Prescriptions for the cure of a disease called Uchetu, characterised by nodosities and pain, and most probably leprosy, are therein contained, and these date, if we accept the authority of Brugsch, from the period of Hesepti of the legendary first dynasty (4600 B.C.), that is, from a time long antecedent to the Mosaic Exodus. Uchetu, in Prof. Macalister's opinion, is probably the same disease as the κέδματα of Hippocrates.

An early Biblical notice of "tsaraath" occurs in Leviticus, chap. iii., in which, however, the description seems to apply better to certain other affections than to "leprosy" as at present understood. In other passages in the Bible also, as in Exodus, chap. iv., we read of "leprous as snow."

Now, the enactments in Leviticus refer chiefly to questions of diagnosis in the first stages of the disease, and whether the sufferers should be made outcasts or not; in this connection we must remember that some of the early cutaneous phenomena of leprosy, as will be seen later, may simulate to some extent the characteristic lesions of such diseases as leucodermia, morphœa, etc. It may be assumed, however, from many allusions in the Bible and other ancient writings, that true leprosy existed largely among the early Jews; although it was doubtless then, as it is now by inexpert observers, confounded with other chronic and severe maladies of the skin, like leucodermia, the syphilides, the tuberculides, frambœsia, malignant growths, and even scabies, eczema, psoriasis, and several other obstinate cutaneous affections.

Leprosy seems to have been also prevalent in ancient days in Persia, where, before the time of Herodotus (*Herod.* i. 136), there were stringent laws for the expulsion of lepers from the towns. Atossa, wife of Artaxerxes II., was said to have been affected with the disease.

In India, leprosy, under the name of "Kushta," was first described by Atreya, who is quoted in the *Rig Veda Sanhita*, a work dating from about 1400 B.C. It appears, indeed, to have been well known long before the accession of Rameses II., fixed by Dr. Mahler at 1348 B.C.

The disease was first recorded in Japan about 1250 B.C.; but China does not seem to be alluded to in the earliest accessible documents. It is believed, however, that it was first noticed in that country one or two centuries before Christ.

It has been surmised that Egypt was really the birthplace of leprosy; that the Jews took it thence, and that by the commerce and wars of the Egyptians it was carried to the far East. The evidence in support of these opinions is very scanty.

In all the countries mentioned above, leprosy has continued to exist until the present day as an endemic disease.

Leprosy is first mentioned in Europe by Aristotle about the year 345 B.C., under the term "Satyria." Hippocrates, indeed, at an earlier date, speaks of *λεπραί*, but the description given doubtless refers to the disease we now call "Psoriasis"; and he also refers to the "Phœnician disease" as the cause of the *Λευκαί* or white affections. In the third century before Christ leprosy had probably become more common in Greece; and at about that time and subsequently it was known chiefly by the names "Elephantiasis" (Aretæus, Galen, Celsus, etc.) and "Leontiasis" (Aretæus). Aretæus, in the first century A.D., gives an excellent description of it.

The disease is believed to have spread in early times from Greece to the neighbouring countries of South-Eastern Europe; and it first attracted attention in Italy during the first century B.C., shortly after the return of the Pompeian army from the East.

Leprosy in the Middle Ages.—It is quite possible that leprosy may have been carried by the Romans to all parts of their vast empire, through their relations on the one hand with Asia and Africa, and on the other with various countries of West and North Europe; at any rate it gradually increased in these countries to such an extent that a few centuries later it was deemed necessary to establish leper asylums—as in Spain, Germany, France, England and elsewhere.

Various expeditions and migrations, subsequent to the fall of Rome, no doubt largely influenced the distribution and exacerbation of leprosy in Europe during the early Middle Ages; the advent of the Moors and the goings and comings of the Crusaders may have had such a direct or indirect effect. The diffusion may to some extent be followed by noting the dates of legislation on the subject, for laws dealing with lepers were enacted in Lombardy in the seventh century A.D., rather later in France—by Charlemagne in 789, and by Noel Dha, King of Wales, in the year 950.

The earliest leper asylums appear to have been established in the eighth century; but the greater number of these institutions, which were rather of the nature of religious houses than of hospitals in the modern sense of the term, date their foundation from the eleventh to the thirteenth centuries. In England the first was founded at Canterbury in 1096; and from that time until the year 1472, when the last was established at Highgate, some 112 such institutions arose in different parts of the country. One of the earliest was in St. Giles', London, and another occupied the site of the present Palace of St. James.

From England leprosy gradually spread to Scotland, and ultimately to the Northern Isles, where indeed it lingered longest. Robert Bruce died of leprosy in 1329. Towards the end of the fourteenth century the disease was rapidly declining in England, and a commission which was appointed in 1470 reported that very few lepers were left in the lazar-houses. Leprosy had practically disappeared from England before the accession of Henry the Eighth, but not from Scotland until much later. The last indigenous leper was seen in the Shetland Isles in 1798, and a case occurred in Edinburgh in 1809.

In France no less than 2000 lazarettos are said to have existed during the thirteenth century, and there were many others in the remaining civilised parts of Europe. Unquestionably a considerable number of the unfortunate inmates of the lazar-houses of the Middle Ages were sufferers from syphilis and various chronic diseases of the skin, for we know that in the beginning of the sixteenth century, when physicians were better acquainted with such diseases, and especially with the diagnostic signs of syphilis, a revision was made of the lazar-houses of France and Italy, and it was then found that in many of them the majority of the inmates were not suffering from leprosy. Taking all the facts into consideration, it must nevertheless be admitted that true leprosy was undoubtedly widely prevalent over the greater part of Europe during the Middle Ages, that it gradually diminished in most of the countries from the fourteenth century onwards, and that it has remained as an endemic disease in certain districts only. The descriptions of the mediæval writers show that the disease was the same then as now.

Geographical Distribution.—At the present time leprosy is widely but unequally distributed over the earth's surface. It occurs as an endemic disease in many places in the tropics, in the temperate zones, and even so far north as the Arctic Circle.

In Europe the principal centres are—(1) in Western Norway, near Bergen, along the borders of the Norde and Söndre Fiords; in the neighbourhood of Molde and Trondhjem, and as far north as Hammerfest and the Lofoten Islands; (2) the countries and provinces on the borders of the Baltic (Finland, Lirland, Courland, etc.); (3) Southern Russia (the province of Kherson, Tauride, the Don Cossack, Cuban and Tersk, Stavropol, Astrachan, and Ural Cossack Districts); (4) Greece (Acarnania, Laconia, Messenia, and the Grecian Archipelago); (5) Turkey (Thessaly, Macedonia, Roumelia); (6) the larger Mediterranean Islands (Crete, Cyprus, Sicily, etc.); (7) Spain (Alicante, Malaga, Granada and Seville); and (8) Portugal (Beira, Estremadura, Algarve). Leprosy is prevalent in Iceland, and even increasing. Ehlers states that the cases are now about 200.

A limited number of indigenous cases are, moreover, still to be found in several other European countries, for example, in Sweden, Italy (the Riviera, Naples), Roumania, Hungary and France (the Riviera, Nice, about the delta of the Rhone, and possibly Brittany).

The European leper asylums now established are situated at Bergen, Molde, Trondhjem (the Norwegian asylums contain now together about 500 inmates), Dorpat (also at Oesel, Rigi, and Lirland — the Baltic provinces), Constantinople, Cyprus, San Remo, Alicante and Lisbon.

In other places where leprosy is not endemic, cases are occasionally met with—as in London, Paris, Vienna, Berlin, Rome, etc., but such patients have invariably acquired their disease as natives or sojourners in some other country in which it persists. Within the last three or four years ten cases have come under my own observation in London.

In Asia leprosy is as widely prevalent now as in ancient times. It occurs in Asia Minor, in Palestine (with an asylum at Jerusalem with about fifty inmates), the mountainous districts of Syria, Kurdistan, Persia, Turkistan, Arabia (especially at Muscat); in Siberia (where in the Yakutsk district there are probably about 100 lepers), Kamtschatka, Japan and China (in the southern and western coast districts). The Chinese leprosy is a matter of some moment to other nations, for emigrants from that country have planted new foci for the extension of the disease in more than one distant place in both hemispheres.

Leprosy exists throughout the Indian Peninsula, being especially prevalent, both absolutely and relatively, in the Burdwan and Kumaon districts of Bengal, and the Bombay part of the Deccan. There are asylums at Calcutta, Bombay, and many other places, but it is estimated that at present not more than 2 per cent of the Indian lepers are thus cared for. It is rare in Scind, common in Ceylon and the Andaman and Laccadive Islands. It is also frequently met with in Burma, Siam, Cochin-China, and the Straits Settlements, where, at Penang, there is a large asylum. Numerous cases occur in Java, Sumatra and the other islands of the East Indian Archipelago, and also in Borneo.

As regards Africa, we find the disease extensively diffused in Egypt, both in the Nile basin and along the shores of the Mediterranean and Red Seas. It is also prevalent in Abyssinia—on the coasts as well as in the plains and hill districts. It occurs in Algiers and Morocco, but here it has probably been more often confused with syphilis. It is found in the Canaries and Madeira, and less commonly in the Azores; and it also exists at St. Helena. On the West Coast it extends from Senegambia to Cape Lopez. It is probably endemic in the interior of Africa, for it is not unfrequently found in slaves from the Soudan and elsewhere. Livingstone met with it in his travels, and there is now a centre in German East Africa. The disease is very common in South Africa, where it is generally believed to be increasing, and a large leper settlement is in active work at Robben Island near Cape Town. Since 1850 an endemic centre has sprung up among the Zulus who had migrated to Natal. On the East Coast cases are found at Zanzibar, Mozambique, and in the islands of Madagascar, Mauritius, St. Marie, Réunion, Rodrigues and the Seychelles.

In Australia cases of leprosy have been cropping up within the last twenty years, chiefly among the Chinese, but also to a less extent among the white colonists. From 1882 to 1891, twenty-seven cases had been under the cognisance of the New South Wales Board of Health; at the latter date there were fifteen in the lazaretto at Little Bay near Sydney—eight being Chinese and seven natives of the colony of European parentage. A rigid system of segregation is at present adopted in this colony, and there are now forty at the institution. A few cases have occurred in Queensland and Victoria.

In New Zealand a small centre has long existed among the Maoris of Taupo and Rotorua. The disease, which is chiefly known by the name of "Ngerengere," is believed to have been introduced towards the end of the seventeenth century; it appears to be dying away. Two cases have been reported among the whites, and one in a Chinaman.

The Hawaiians, in proportion to their numbers, are probably more afflicted with leprosy at the present time than the inhabitants of any other part of the world. The leper settlement at Molokai was established in 1865, shortly after a manifest increase had been observed in the number of cases throughout the islands; from that date to 1876 1570 lepers were received. The average number of the leprous population in the settlement for some years has been upwards of 700.

The disease is also known in the Philippines, Fiji, Tahiti, and other islands of the Pacific, but information on the subject is scanty.

The western hemisphere was first invaded by leprosy in the seventeenth century—indeed from the time of the importation of negro slaves from Africa. It is also probable that some cases came from Portugal and Spain. In certain parts of America and in some of the West Indian Islands the disease is at the present time very common; other places, on the other hand, are quite exempt. There are two endemic centres in the northern continent, at Louisiana and at Tracadie, New Brunswick. In the former district it appears to be increasing, while in the latter it has decreased during the last few years.

The disease is also to be found among the Chinese in California, and among the Norwegians of Minnesota, Wisconsin and Dakota. In neither case is there evidence of its spreading. The Norwegian lepers, in fact, have diminished from 160 known cases to about a dozen.

In Central America leprosy is generally diffused in Mexico and Costa Rica, and occasional in Nicaragua.

In South America it is especially common in British and French Guiana, less so in Dutch Guiana. Brazil is largely infected, and it also occurs in North Argentina and Paraguay. There are cases in Ecuador, very few in Peru, and apparently none in Bolivia and Chile. It is common in Columbia and Venezuela, and in several of the West Indian Islands, for example, Jamaica, Barbados, Trinidad, Cuba and Hayti.

Varieties of Leprosy.—Although leprosy, undoubtedly, is a fairly definite disease, the cases may be conveniently grouped under at least two, possibly three, categories—according to certain predominating *clinical* characters; thus we have the so-called "varieties" or "forms" of leprosy, namely, (1) the *nodular* (also called "tuberous," "tuberculated," etc.); (2) the *smooth* (also called "anæsthetic," "non-tuberculated," "trophoneurotic," etc.); and (3) the *mixed*. In the first the skin is primarily and chiefly affected; in the second, the nerves are most implicated; and in the third, both the skin and nerves are more or less extensively diseased. These three varieties are not distinct processes, for the two first often pass into each other; most tuberous cases, indeed, at some time or other exhibit peripheral anæsthesia, and often terminate in "mixed" leprosy; and more rarely the so-called anæsthetic form may develop "tubers" on the skin. This artificial classification is only adopted here for convenience of description. The "mixed" form is by no means universally accepted as a variety, as it is but the complete manifestation of the disease. "Macular" leprosy, also spoken of formerly as a variety, is merely an early stage. "Lepra mutilans" and other names have been given to cases which present particular features.

The percentage of the three forms varies much in different places, as shown in the following table:—

	Trinidad. (Bake).	Demerara. (Hillis.)	India. (Commission.)	Norway. (Danielssen.)
Nodular . . .	36	21	12·2	51·6
Smooth . . .	44	62	56·6	33·3
Mixed . . .	20	17	31	15·1

It is urged by Hillis and others that the three forms run their course each in a peculiar manner; and, as will be seen below, it is true that the clinical features in the two chief classes of cases differ throughout the progress of the disease in important particulars, the differences depending upon the order of invasion of the tissues.

Symptomatology.—*Nodular Leprosy.*[1]—"Tuberculated," "tubercular," "tuberculous," "nodular-dermal," "dermal," "cutaneous," "hypertrophic" leprosy. Lepra tuberosa, L. tuberculata, L. tuberculosa, L. dermoplastica, Lèpre systematisée tegumentaire.

At the onset of this form of the disease the patient suffers more or less from prodromal symptoms, such as irregular rises of temperature, rigors, lassitude, drowsiness, dyspepsia, diarrhœa, headache, vertigo, epistaxis and profuse perspiration. These phenomena may be very slight, or they may be in part or altogether absent. Even when well marked they cannot be regarded as characteristic of leprosy; they are such as may precede any specific febrile disease.

The first positive indication of the disease is the appearance of the leprous eruption, which shows itself as a slightly raised, irregular, shiny, erythema-like patch of a reddish or copper tint in white or light coloured races, and of a colour which hardly differs from that of the surrounding skin in negroes and the darker races. There is from the first distinct infiltration of the derma, and there is usually some hyperæsthesia. The parts which are generally at first affected are the lobes of the ears, the alæ of the nose, the malar prominences, the forehead, the eyebrows and root of the nose, the lips and chin. Later the eruption appears on the limbs (especially on the forearms), thighs, and buttocks.

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[1] As the terms "tubercle," "tubercular," etc., have now a distinct and universally acknowledged pathological meaning in relation to a different disease—tuberculosis—I venture to suggest that we should cease to employ them or their derivatives in connection with leprosy.—P. S. A.

These patches may persist, or some or all may decrease in size, and so far disappear as to leave the skin at its original level, with only a slight brownish discoloration. In some cases the eruption may vanish altogether—giving rise too often to illusory hopes of cure. After a time febrile symptoms again occur, and a fresh crop of eruption breaks out. This may happen several times before the appearance of the typical leprous nodules—the so-called "tubercles"—which mark the second stage of the disease. These show themselves as small papules which gradually enlarge to the size of a pea, or in the course of time even to that of a pigeon's egg. They usually appear first on the site of the former eruption, but they may also arise on parts of the body hitherto unaffected. They are tense, shiny masses, reddish brown in fair subjects, and rather darker than the surrounding skin in the dark races. In the former small blood-vessels may often be seen over the nodule, beneath the tightly stretched integument; and in the latter, whose skins are normally greasy, the openings of the largely developed sebaceous glands are usually evident and plugged with dirt.

As time goes on, parts of the body free from the original eruption become invaded by the new growths. They appear on the hands and fingers, feet, shoulders, arms, and more rarely on the back, neck, chest, abdomen, palms and soles. Thickening of the skin on the elbows and knees is not uncommon, but discrete nodules here are rare. The hairy scalp is very rarely affected. The male mammary gland often becomes enlarged and the nipple nodulated. The prepuce also is often thickened and infiltrated by the new growth, and micturition may be impeded; the glans does not usually appear to be affected. Loss of hair from the eyebrows is often observed early in the case. The fingers and toes are frequently swollen and tapering without actual nodulation, and the nails break off in flakes. The skin of the shins may become tense, shiny and painful.

Four distinct varieties of leprous infiltration may in these cases be recognised clinically:—

(*a*) The original nodules above described may remain discrete, without diffuse infiltration of the skin.

(*b*) The nodules may coalesce into large irregular nodose or flattened masses, varying from one to many inches in diameter.

(*c*) Diffuse infiltration may occur from thickening of the original leprous patches.

(*d*) In rare cases subcutaneous small hard nodules may form, the skin being freely movable over them.

Two or more of the above varieties may coexist in the same patient.

The eye is often involved in this form of leprosy; the conjunctiva may then be more or less infiltrated, enlarged blood-vessels are usually seen, and the new growth may implicate the cornea extending from the periphery and ultimately reaching into the anterior chamber. There may be severe pain, and sight may be destroyed. The iris and ciliary body also may become invaded, and even the choroid and retina, and the eye thus eventually changed to a shapeless mass, which may increase to such a size that the eyelids cannot cover it. Both eyes are often affected, one after the other.

The mucous membrane of the nose becomes thickened, and sometimes nodules are formed in it, giving rise to snuffling and nasal intonation. Nodules are occasionally found inside the cheeks and on the fauces; and frequently on the epiglottic, ary-epiglottic folds, the vocal cords and ventricles of the larynx. They have been seen occasionally in the trachea and bronchi, the uterus and vagina.[1]

When the nodules are fully developed, the hyperæsthesia which accompanied the initial eruption is replaced by diminished sensation and even by complete anæsthesia, the result of pressure on the ends of the nerves. At this stage also infiltration of the nerve-trunks often occurs.

The further history of the nodules varies. In some cases they remain almost stationary, or increase very slowly; in others they disappear altogether, leaving wrinkled areas of skin, and some persistent anæsthesia and deformity.

The face now acquires the characteristic leonine aspect, the skin of the forehead being greatly thickened, the natural furrows exaggerated and the eyebrows prominent, the face thus having a sombre expression. New growths sometimes form in the eyelids and hang down over the eyes. The cheeks are often puffed out and pendulous from the weight of the deposit. In some cases, however, the nodules may remain small and discrete, and cover the nose, lips and chin as well as other parts of the face. The ears are usually much thickened and nodulated, the lobes being especially liable to infiltration, with consequent enormous enlargement.

In the largest class of cases the new growths increase very rapidly; fresh crops suddenly appear from time to time, each outburst being accompanied by a rise of temperature to 102° or 103° F. Several such attacks may occur in the course of a year; and during their advent the lymphatic glands, especially the femoral, become painful and swollen. When the fever has passed off, more or less enlargement of the glands may remain. Some recession of the older tubers may be apparent after the attack, but the total amount of leprous deposit is increased at every exacerbation. The hands and feet often become covered with masses of new growth which are easily injured on movement or by pressure and the like; the resulting sores are difficult to heal. The nails drop off, or are converted into distorted horny pegs.

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[1] Dr. Rake has not seen them in these positions although he made many autopsies.

The condition of the sexual organs varies. If the disease be fully developed in males before puberty, the testicles usually remain small and imperfectly developed, and the sexual power is absent; when the onset of the disease takes place after puberty, although at first there may be increase of sexual desire and power, testicular atrophy and impotence generally follow. In leprous women there is probably a like effect: although by no means always sterile, in most cases they bear few or no children, and their offspring are often, but not always, weak and puny, and die early.

After the stage of nodulation has lasted for a variable period the final stage of ulceration sets in, and the growths on the more exposed parts, like the face, ears, hands and feet, are usually the first to ulcerate. In favourable cases, and with proper attention to cleanliness, these ulcers may heal and a partial spontaneous cure be established, the patient living for years afterwards, much disfigured by irregular areas of cicatricial tissue but with no fresh development of nodules. Occasionally, as the result of cicatrisation, the mouth becomes so contracted that the tongue cannot be protruded, and feeding becomes difficult. Sometimes the ulcers on the feet and hands become the seat of large warty masses.

In other cases the ulcers refuse to heal, and spread till they form large irregular tracts of ulceration on the legs, buttocks, forearms, etc.,—sometimes more or less enveloping a limb. Large florid bleeding granulations often spring up on the ulcerating nodules, especially on the hands and feet. After living for months or years in this state, the patient dies from simple exhaustion, kidney disease, tuberculosis, or other visceral complications.

In a third class of cases the progress of events is more rapid. The ulcers become phagedænic, especially on the fingers and toes; the sloughing extends, gangrene of one or more extremities follows, and the patient soon dies of exhaustion or pyæmia; but this latter termination is not so common as in the other forms of the disease.

During the course of the cutaneous ulceration just described, other symptoms are often present as the result of ulceration of the mucous membranes. Great pain and photophobia and eventual blindness from corneal opacity follow ulceration of the corneal nodules, even if the latter have not already invaded the rest of the eye. Pain and difficulty in eating and swallowing accompany ulceration of the lips, tongue, and fauces, while as the result of the breaking down and cicatrisation of the growths of the epiglottis and larynx, the voice becomes croaking, and sometimes reduced to a whisper.

The patients also suffer from painful attacks of dyspnœa, which sometimes prove fatal.

Smooth Leprosy.—"Anæsthetic," "non-tuberculated," "trophoneurotic," "atrophic," "nerve leprosy," "Danielssen's disease," *Lepra glabra*, *L. anæsthetica*, *L. maculo-anæsthetica*, *L. nervorum*, *L. neuroplastica*, *Lèpre systematisée nerveuse.* The prodroma of the cases in which anæsthesia and trophic changes are the most prominent features are less marked than in those just described, and they may be so slight as to be overlooked. Feelings of chilliness, depression, and indefinite malaise are often noticed. The patient may experience shooting pains in nerves, especially the ulnar and peroneal, a burning and tenderness along their course, and hyperæsthesia of the skin of the parts they supply. These pains may be absent, and the first evidence of the disease may be the numbness of the hands and feet, and diminished power of grasping. There may be difficulty in holding tools during work, accidental burns and wounds may take place without cognisance, and when the patient walks he may feel as if treading on wool.

In other cases the maculæ are the first symptoms noticed. These spots, which generally appear singly, are of three kinds: (1) those which begin with erythema, (2) those which begin with pigmentation, and (3) those in which there is a diminution of pigment either initially or rapidly following an excess of the latter. The spots are usually of a light copper or brown tint in fair skins, or of a dirty yellow in the blacks, and one or two inches in diameter; they differ as a rule from the primary eruption of nodular leprosy in not being raised above the surrounding skin. At this stage they are generally neither hyperæsthetic nor anæsthetic, but the sweat secretion may be locally absent.

This eruption usually appears first on the shoulders, back and loins, buttocks, thighs, knees and elbows, and on the face; but the face often escapes altogether. Sometimes it occurs on the course of certain nerves, such as the musculo-spiral and ulnar. Fresh patches continue to appear, but the patient's general health may be unaffected—no special symptoms being observed. It often happens, however, that about this time anæsthesia of the skin supplied by the ulnar nerve is apparent; and the fourth and fifth fingers may begin to contract—more commonly in the left hand.

The next stage of the disease is characterised by the spreading of the eruption. After the original spots have remained unchanged for a year or two they begin to enlarge peripherally. The centre fades to a dirty white or pale yellow, and at the same time becomes anæsthetic. The hairs fall out, and the patch becomes wrinkled and dry from the destruction of the sweat glands. The border is now slightly raised, is of a reddish brown colour, and may be studded with small papules, which sometimes become vesicular. In rare cases the vesicles increase in size and become pustular. Desquamation is always more or less present as the patch grows, the scales being thin and powdery about the centre, and larger at the periphery. If vesicles or pustules be present, they burst and leave scabs which eventually fall off. Individual spots may increase greatly in size, or neighbouring ones may coalesce into large serpiginously bordered tracts; and immense areas of the integument—for example, the whole of the skin of the back or thighs—may thus become changed. The face is sometimes completely thus invaded, the area extending from the margin of the scalp to below the jaw, and imparting to a negro the physiognomy of a half-caste.

The more superficial nerve-trunks may now, or perhaps at an earlier stage, be felt enlarged beneath the skin, especially the ulnar above the elbow.

With the spread of the eruption the anæsthesia increases, until in some cases the whole of the upper or lower extremities, or more rarely the greater part of the body and limbs, becomes lost to feeling.

Anæsthesia may also be present beyond the area of the patches, even when the latter retain a certain amount of sensation. There are also cases in which there is anæsthesia of the mucous membrane of the mouth and pharynx.

When the active spreading stage is over, the margins of the spots fade in colour and regain the level of the surrounding skin.

In white patients it is sometimes difficult to distinguish any difference of colour between the anæsthetic patch and the rest of the skin. A Frenchman under Dr. Rake's care in Trinidad exhibited no variation of tint until four years after the onset of the disease: the patches then became mapped out by congestion of the surrounding skin. In rare cases there may be no skin eruption.

The final stage of permanence is now reached. After the eruption has ceased to be active, or when there is no further deposit in the nerves, the disease may remain stationary for a number of years—the only evidence of the disease being the remains of the eruption, and more or less contraction of the fingers. In the majority of cases, however, paralysis and destruction of tissue progress, as the result of the increased amount of new growth in the nerves.

The contraction which has already been mentioned, as commencing in the third and fourth fingers, extends to the other digits—in less degree, perhaps, in the case of the thumb,—the second and third phalanges being flexed towards the palm, so as to give the extremity a claw-like appearance. The interossei and the muscles of the thenar and hypothenar eminences at the same time become wasted. Similar changes, but less marked as a rule, take place in the lower extremities. As a later effect there may be wrist-drop, and more rarely atrophy of the muscles of the leg, giving rise to a flail-like condition of the foot; and occasionally there is effusion into the wrist and ankle joints, with erosion of cartilage and dislocation of the bones, exactly resembling Charcot's disease. Ulceration frequently now ensues, either as the result of bursting of large bullæ on the hands and feet, or as the effect of mechanical injury to the anæsthetic parts. The patient may take up a hot cup or pipe without feeling it, step on a sharp stone and the like, thus producing wounds which break down into perforating ulcers. More commonly, however, this form of ulcer begins as a bulla which, prevented from early rupture by the thickened epidermis of the sole, burrows deeply into the tissues. Ulcers are especially common on the fingers and toes; and the nails often split and break, or are changed into talon-like appendages.

The bones become necrosed, and are cast off whole or in pieces; or in other cases interstitial absorption of bone takes place, and the finger or toe becomes shortened, the remains of the phalanges ultimately becoming ankylosed. In whatever way the bones be removed, a portion of the nail usually persists as a horny peg attached to the end of the stump. Destruction of the bones of the carpus and metacarpus is rare; but in the lower extremity the necrosis often involves the other bones of the foot as well as the phalanges—especially the metatarsals and calcaneum. Occasionally all the distal parts of both lower and upper limbs are removed in this way, as if amputation had been performed. Rare cases have been described in which the caries has extended beyond the wrist and ankle joints, and the epidermic remains of the digits have been seen even as far up the limb as the elbow-joint.

Ulcers over the knees, shins, elbows, and other parts of the body also occur, but much less frequently than in nodular leprosy; cracks often open on the palmar and plantar aspects of the digits, beginning in the grooves beneath the joints, spreading transversely, and forming chronic ulcers. Suppuration may extend along the sheaths of the tendons, with resulting necrosis of the latter as well as of the bones. In other cases a furrow may form between the joints, and by gradual deepening produce a condition resembling ainhum. Though the ulcers of "anæsthetic" leprosy are for the most part painless, distressing neuralgia may accompany perforating ulcers of the foot; and in other cases there may be intense pain in the sciatic, ulnar, supraorbital and other nerves, due to the interstitial deposit. The patient, moreover, often complains of feeling cold. The ulcerations sometimes spread rapidly, and become gangrenous, all the tissues being affected, and a line of demarcation formed. The gangrene may be limited to one or more of the fingers or toes, or the whole hand or foot may be involved; in rare cases it may extend farther up the limb. As a result of hard labour, handling tools, etc., suppuration may be set up in an anæsthetic finger, and may travel up the tendons and burrow into the muscles as far as the elbow. Towards the end of life symmetrical bed-sores sometimes form rapidly over the buttocks.

The affections of the eye in this form of leprosy are mainly the results of lesions of the fifth and seventh nerves. Ophthalmia is not uncommon, and ulceration of the cornea frequently occurs which may lead to pannus, onyx, hypopyon, iritis, and occasionally to the destruction of the whole eye. There may be ptosis; and paralytic ectropion is often seen, with facial paralysis of the same side. The surface of the cornea may be quite anæsthetic without any of the other evidences of disease.

Sexual desire is not as a rule increased in smooth leprosy; the power of procreation, on the other hand, is retained until a comparatively late period.

"*Mixed*" *Leprosy.*—Gerlach's dissections indicate that all leprosy is "mixed" from a very early period; for, according to that observer, the primary growth in the smooth form takes place in the skin around the peripheral ends of the nerves, and travels up to their trunks. Assuming the correctness of his researches, it is nevertheless a fact, that in the majority of cases the early skin changes do not, as we have seen, present quite the same appearances as in nodular leprosy.[1] Moreover, in a large number of cases anæsthetic patches and other evidences of nerve infiltration coexist with definite cutaneous nodules, and we may therefore, for clinical purposes, class such cases together under the appellation of "mixed leprosy." Such cases may also be considered under three heads :—

(1) Those in which the leprous infiltration is for a long period confined to the skin, and subsequently advances in the nerve-trunks.

(2) Those in which the symptoms of nerve implication are for a considerable time manifested alone, the formation of dermal nodules being subsequent; and

(3) Those in which the leprous dermal infiltrations and the various symptoms of nerve-trunk implication are observed together from a very early period of the disease.

Of these the first class is by far the most numerous, and, indeed, so often do the nerve-trunks become involved in advanced cases of nodular leprosy, that we may regard a leper with this latter form of the disease as one who has not lived long enough to develop "mixed leprosy," which is the complete or generalised affection.

The second class of cases, in which nodules develop late in the course of neural leprosy, is undoubtedly rare. In ten years' experience at Trinidad only three instances were noticed. Leloir also only mentions three cases.

The third class is less uncommon, and it often happens that early cutaneous infiltrations almost or quite disappear, there remaining only anæsthesia, deformity, etc. It would be sometimes, in such cases, difficult to believe that the patient's skin had ever been nodulated were it not for the presence of flabby, wrinkled patches on the ears, cheeks, and other sites of the former nodules.

A detailed account of the symptoms of "mixed" leprosy is unnecessary, for they consist of a combination, in varying proportions, of the phenomena already described.

In the Trinidad Asylum, during a period of eight years, phthisis and other forms of visceral tuberculosis were immediately responsible for 20 per cent of the deaths among the nodular cases, for 19 per cent of the deaths among smooth cases, and 25 per cent of those among the "mixed" cases; various forms of kidney disease caused 30 per cent of the deaths among the nodular cases, 27 per cent among the smooth, and 10 per cent among the mixed; tuberculosis and renal affections combined were responsible for 14 per cent, 3 per cent, and 10 per cent of the deaths respectively; and the leprosy itself, or exhaustion from leprous ulcerations, gangrene, pyæmia, asphyxia, due to obstruction of the larynx, and accidental complications, were ascribed as immediate causes of death in 36 per cent of the nodular, 51 of the smooth, and 55 of the mixed lepers. Observations in the same asylum extending over 18 years showed the average age of onset to be 21½ years, 30½ years, and 25¼ years in the three classes of cases respectively.

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[1] Hansen does not recognise this distinction, although he admits that the patches of the tuberous form are certainly usually thicker, indicating a greater degree of infiltration than the anæsthetic.

The Incubation of Leprosy.—Many instances are on record which show that the virus may remain latent in the body for many years without giving rise to any of the symptoms of the disease. In the present state of our knowledge it is impossible to speak of any definite period of incubation in connection with leprosy. We do not know whether its entrance is marked by any initial lesion; for although in a few exceptional cases some slight traumatic injury, with subsequent local inflammation and difficulty of healing, was observed at a variable interval before the disease was suspected, yet most of the patients are unable to point to any circumstance of the kind, or to give any notion of the date of initiation.

Instances have been given of the appearance of the disease only a few weeks or months after the patient has come from an unaffected to an affected district; and there are others in which the pathognomonic signs have not been observed until forty years after the individual has been in a leprous country, or could possibly have been in contact with lepers. There is a case now in London of such retarded incubation, and another Englishman, lately under my care, showed no mark of the disease for eleven years after coming back from India, whither he had been taken as a child. Since his return to this country he has been living in a small country town, and has had no relations with the East, or with any one or anything therefrom.[1]

Pathology of Leprosy.—*Anatomical Changes.*—Post-mortem examination, or the observation of excised parts during life, in every case reveals the fact that the ultimate phenomena described above are due to the development of the characteristic leprous neoplasm in certain tissues of the body. This new growth is largely composed of bacilli-bearing "lepra-cells."

The state of some of the more important organs commonly affected may be described, and a full description given of the neoplasm as observed in the skin.

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[1] Such a case is known to me. Ten or twelve years ago a gentleman, then aged about forty-two (a married man, by the way), who had suffered a good deal of privation as a sportsman in the East, consulted me for numbness and pains. The ulnar and other nerves were plainly traceable by the finger for long distances on both hands, and there were anæsthetic patches. At my request he consulted an eminent authority on leprosy, whom I had previously warned to give the diagnosis to me only. He agreed with me that the case was one of early but well-marked leprosy. To the patient's surprise, we made him throw up his appointment and forbade him to return to the East under any circumstances. He is now well, and ignorant of his malady; I have not examined him for some years, as he declares himself to be well, and it is best for him not to have his attention drawn to himself. Fifteen or twenty years ago a young medical man showed me his own fingers, which, on the ulnar sides of the hands, were contracted and anæsthetic. He was born in South Africa, and took leprosy as a child. He has lived in England since childhood, and believes himself to be quite "cured."—Ed.

The Skin.—A young or growing nodule of the skin when cut into shows the epidermis normal, but the corium rather firmer than in healthy skin; a little viscid fluid can be squeezed out. In the older growths the cut surface is granular, and of a yellowish white colour, and the substance is softer. The subcutaneous tissue is also sometimes infiltrated, and has a gelatinous appearance; but, instead of softening with age, becomes firmer. Occasionally a diffuse infiltration is developed only in the subcutaneous tissue. The walls of the vessels are thickened by the deposition of a lardaceous-looking mass, and the nerves are also increased in size by the same deposit, and by the existence of a definite neuritis.

The sweat glands, the sebaceous glands, and the hairs are gradually compressed by the surrounding leprous infiltration, and finally they quite disappear. In some cases hypertrophy of the arrectores pilorum seems at some time to take place, and at first there may be also hypertrophy of the sebaceous glands and an increased secretion of sebum.

As the growth increases towards the surface the epidermis is pressed upon and becomes attenuated.

The deeper parts of the subcutaneous tissue and the subjacent tissues are at first not directly involved.

Under the microscope, a vertical section of a cutaneous nodule exhibits, in place of the normal connective tissue which has become altered or destroyed, a large collection, or several clusters, of characteristic lepra-cells, forming a mass which is situated more often in the middle or deeper layers, but sometimes also in the upper and papillary layers of the corium. In the older growths, which extend almost to the surface, the papillary body becomes thinned with obliteration of the papillæ and thinning of the rete mucosum; but in early nodules the latter with its interpapillary processes may be intact, and a band of unbroken connective tissue may be seen between it and the affected part of the corium.

The masses of cells thus constituting the nodule are at first principally grouped around the vessels, nerves and glands, and they can be seen to extend along the course of the lymph channels. In the instance of a subcutaneous nodule from a prepuce examined by myself, the mass was largely made up of the immensely thickened blood-vessels, which, as they entered the nodule, showed a dense infiltration of their adventia, media and intima, with obliteration of the lumina.

The so-called "lepra cells" are very similar in superficial appearance to the granulation cells of lupus, syphilis, etc. They vary in size from that of an ordinary leucocyte to four times that size or more, and, when stained with hæmatoxylin or by ordinary histological methods, they exhibit one or sometimes two nuclei. As will be seen directly, they can always be shown to contain specific bacilli in greater or less numbers.

Occasionally very large multinucleated cells, somewhat resembling the "giant cells" of lupus, are seen in the peripheral or deeper parts of the growth; and these may have arisen in several ways, for example, by the continued growth of one cell and subsequent proliferation of its nucleus, or by the swelling and coalescence into one mass of the endothelial lining of a small vessel or capillary. The larger ones are often vacuolated. Hansen and Thin believe that when true "giant-cells" are seen, the growth is tuberculous and not leprous; and that those seen by myself were cross and oblique sections of blood-vessels containing corpuscles. Thoma, Benoir and Boinet and others, however, have also described large multinuclear cells as occurring sometimes in the leprous neoplasm.

Besides undergoing fibrous degeneration, fully-developed tubercles may exhibit desquamation, vesicles or pustules on their surface, or they may ulcerate and become covered with crusts. The sections show that during desquamation the stratum granulosum and eleidin have diminished or disappeared, but that there is little change in the greater part of the cells of the stratum corneum. Vesicles and pustules, on the other hand, are produced by a raising of the whole epidermis or by cleavage of its layers. When ulceration has set in there is rapid destruction of the nodule, and cells and detritus are thrown off in great quantity.

Sections taken from one of the erythematous macules in an early stage of the disease showed an infiltration of the corium with an irregular cell growth, in which some large multinucleated cells were also scattered. In these sections no bacilli were observed.

The microscopical examination of a portion of skin excised from an anæsthetic patch of a case of smooth leprosy of two and a half years' standing showed principally a general fibroid degeneration of the corium with more or less obliteration of glands, ducts, hair follicles, nerves and vessels. In sections from a more recent case the degeneration was less complete, and there was a more extensive infiltration, especially near the vessels, of an irregular cell-growth; no bacilli were seen. I have given more detailed accounts in Hillis's book.

Mucous Membranes.—The neoplastic lesions of the mucous membrane of the mouth and throat are very similar to those of the skin, but the nodules are softer in consistence, and usually of a pale red or livid colour, or sometimes dull gray and opaline. They ulcerate more readily.

There are two chief varieties of the leprous tongue. In the first, the dorsum may be covered with discrete nodules, varying in size and quickly ulcerating, and separated by furrows. Under the microscope the new growth is made up chiefly of embryonic cells, with comparatively few typical "lepra cells," and their vascularity is slight; in many parts they show fibrous degeneration. The growth may be seen extending through the mucosa and submucosa to the muscles, the fibres of which are separated and destroyed. In the second, the dorsum is occupied by a diffuse leprous infiltration, and divided into raised areas by longitudinal and transverse grooves; the epithelium often becomes detached in grayish flakes. The neoplasm in these cases is almost entirely composed of the lepra cells, and there is no tendency to fibrous degeneration. As the result of ulceration and cicatrisation of the growth in the lips, the mouth may become extremely stenosed and incapable of being opened.

The leprous infiltrations of the pharynx, larynx, and other mucous membranes exhibit very similar microscopical characters. The edge of the epiglottis is often affected very early, becoming thickened and lobulated; and ultimately many of the ligaments, muscles and cartilages of the larynx may become infiltrated with new growth, leading to ulceration and cicatricial contraction. In this way, as well as by occlusion from projecting nodules, the glottis may become stenosed.

Nerves.—The nerve-trunks most frequently invaded by the leprous growth are the median and ulnar in the upper extremity, and the posterior tibial and peroneal in the lower. The facial and the radial are also commonly invaded. According to Danielssen the cutaneous palmar nerve is the first affected; but, indeed, any nerve may be attacked sooner or later. Leloir describes three cases in which the recurrent laryngeal was affected, and he thinks that in this way the aphonia so often present may sometimes be produced. It can be shown that the discoloured and anæsthetic patches of skin are in direct relation to deposit in nerves supplying the parts, and their irregular distribution is explained by the fact that only certain groups of fibres may be implicated. To the naked eye the diseased nerve shows along its course fusiform, reddish gray swellings, often marked with yellowish streaks of fatty degeneration; and the deposit may have a translucent or gelatinous appearance. These thickened segments may be twice or four times the diameter of the rest of the nerve-trunk, and they are often larger where the nerve is more superficial, for example behind the internal condyle of the humerus, or below the head of the fibula, in which positions they can frequently be felt by the observer's finger.

Microscopically the leprous neuritis is similar to that mentioned in connection with the nerves passing through a cutaneous nodule. The swellings are due to the presence of numerous lepra cells, which infiltrating the perineurium produce perineuritis; they are also to be seen situated in the endoneurium, and between the individual nerve fibres, giving rise to neuritis and degeneration. Hyaline thickening of the neurilemma may ensue, the axis-cylinders become disintegrated, and the whole fibre altered. In old-standing cases, in which the activity of the disease has been arrested, the nerve-trunk may be atrophied, and represented only by a cord of fibrous tissue.

Lymphatic Glands.—The lymphatic glands are sometimes invaded, when they may be enormously enlarged, the deposit reaching them through the lymphatic vessels coming from the parts affected—especially in the nodular cases. Those most frequently engaged are the femoral glands—from absorption of deposit from nodules or ulcers in the lower extremity, and the cervical—from disease in the larynx, etc.; but the axillary, bronchial, mesenteric, lumbar, etc., glands may also be affected. It must not be forgotten, however, that these glands, especially those connected with viscera, are also frequently enlarged from concurrent tuberculosis. Under the microscope the adenoid tissue is seen to be more or less replaced by lepra cells; and in old cases there is sclerosis, with thick bundles of connective tissue. Caseation, moreover, may take place,[1] and occasionally the whole gland may suppurate.

The Testes.—The testicle is often the seat of leprous deposit, although in some cases there may be no naked eye appearance of its presence; the gland is sometimes, however, tough and hard to cut. The microscope shows an increase of connective tissue, with the typical cells among the fibres.

The Liver.—To the naked eye no change in this organ may be apparent; the leprous growth, which is sometimes present, occurs as a diffuse infiltration, principally in the interlobular connective tissue, and causes a mild form of interstitial hepatitis.

The Spleen. — No naked eye changes are here present, but bacilli-bearing cells may be found in profusion.

The remaining abdominal organs likewise show no well-marked alterations to the naked eye.

The Spinal Cord. — Danielssen and Boeck described sclerosis and meningitis of the cord; Tschivilow found changes in the posterior cornua —the gray matter opaque and granular, the vessels lessened in number, and a cellular infiltration of the lymphatic sheaths; spinal lesions have also been alluded to by other pathologists. On the other hand, many observers, including Hansen, Neisser and Rake, have failed to find anything definite in the spinal cord. The ataxia sometimes present in advanced cases may be due to lesions in the posterior cornua, independently of leprosy.

Having now given an account of the grosser specific changes in the various organs in the disease under consideration, brief mention may be made of certain affections, whose precise relation to leprosy is not as yet clearly understood.

Tuberculosis is extremely common in lepers. In the last 109 autopsies at the Trinidad Asylum tubercle of one or more serous membranes was found in 33 instances, or in 30 per cent. Guinea-pigs inoculated with material from the autopsies readily manifested tuberculosis. As the deaths from the latter disease at the Trinidad General Hospital during the same period were only 18½ per cent, we may assume that lepers are more liable to tuberculosis than other people.

Kidney disease is even more frequent. In the same 109 autopsies 35 of the cases, or 32 per cent, showed some form of nephritis; while in the General Hospital only 7½ per cent of the deaths were due to nephritis. In none of the kidneys of the above-mentioned 35 cases was there any specific leprous invasion. The disease was probably due to the increased strain thrown on the kidneys by the destruction of the sweat glands so common in leprosy.

Absorption from leprous ulcers or abscesses sometimes produces pyæmic infarcts in the viscera, and sometimes lardaceous changes occur, especially in the liver and spleen.

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[1] Hansen maintains that caseation never occurs in the leprous tissue—where it is seen he considers that it indicates tuberculosis.

Hillis and Arning have described specific ulceration of the large intestine in leprosy; but in Trinidad, when such ulcers were present, they seemed to be associated with kidney disease, or due to causes unconnected with leprosy.

Bacteriology of Leprosy.—That leprosy is due to the presence in the system of a specific micro-organism is now admitted by all pathologists. Its discovery was made by Armauer Hansen in 1871, although a suspicion of the existence of something of the kind seems to have been in the minds of other observers before that date. Both Virchow and Vandyke Carter had called attention to the presence of granular matter in the typical "lepra cells," and Manson had actually attempted the cultivation of the "germ" which he believed to exist in the cells and juice of the nodules; but the Norwegian investigator was the first to recognise in the granules the microbe which he named the "Bacillus lepræ."

In 1880 Hansen published a full account of his observations and experiments, with drawings of the bacillus. In the same year Neisser, working at the San Lazaro Hospital, Granada, and employing the new aniline dyes, placed Hansen's discovery beyond doubt; within the next few years the bacilli were found in leprous material from all parts of the world. It may now be affirmed that the bacillus is existent in the body of every leper at some period, at least, of the disease, and that it never occurs in the bodies of those who are not lepers.

Morphology.—The organism is a rod-like, vegetable parasite, belonging to the Schizomycetes or fission fungi. Its length is a half to three-quarters the diameter of a human red blood corpuscle, and its breadth about one-fifth of its length. Each rod has an outer mucilaginous envelope, the innermost layer of which retains the aniline dye, and thus the internal structure of the bacillus may be obscured. There can, however, be made out with very high powers, within the substance of the bacillus—

(1) Highly refracting oval spores; (2) ordinary protoplasm; and (3) granules.

With certain reagents, such as iodine, strong sulphuric acid, borax-methyl-blue, hæmatoxylin, and osmic acid, these granules colour deeply, the protoplasm remaining unstained. A beaded appearance may thus be produced.

Hansen considers that the "spores" and "granules" are merely evidences of the disintegration of the bacillus. In spite of the fact that spores have been discovered within the bacillus they have not as yet been seen free. The parasite multiplies by transverse fission, and it has been said to be motile.

Although the bacilli of leprosy and of tubercle resemble one another in certain respects, especially in their staining properties, they differ materially in others. When stained with a solution of fuchsin, or some other aniline dyes, in water containing aniline oil (or 5 per cent of carbolic acid), they can both be exposed to the action of certain mineral acids for a short time without being decolorised; thus they differ from all other known bacilli, which when brought into contact with the acid immediately lose their stain. If, however, a simple watery solution of fuchsin be used, the leprosy bacilli alone will retain the stain after immersion in dilute nitric acid. Other points of difference are as follows:—

(1) Leprosy bacilli are generally present in sections in immense numbers, and not sparsely scattered as are those of tubercle; (2) they occur in dense masses held together by the substance they secrete, and are not usually solitary or in small groups; (3) they are always straight and never bent, as are sometimes the bacilli of tubercle; (4) their typical position is in the lepra cells and not in giant cells; and (5) according to photographs taken by Andrew Pringle, they may be club-shaped at one end and tapering at the other, and not fairly uniform throughout like those of tubercle.[1]

Although they can be shown by treating fresh tissue with solution of potash, and by various aniline dye methods, they are best demonstrated in the following manner:—

(1) The juice expressed from a nodule, or the discharge from a leprous ulcer, is smeared over a thin cover-glass, dried and fixed as a thin film by passing through a smokeless flame; or a thin section of a leprous growth may be spread out on the cover-glass; (2) the latter, with the dried material upon it, is immersed or floated face downwards for about twelve minutes (sections may require a longer time) in warmed Ziehl's solution, prepared by adding to distilled water 100 c.c., carbolic acid 5 grammes, alcohol 10 c.c., and fuchsin 1 gramme;[2] (3) the preparation is then decolorised by placing it for a few minutes in 25 per cent nitric acid; (4) subsequently it is passed through 60 per cent alcohol; and (5) finally well washed in distilled water.

The cover-glass may now be examined at once in water; or, better, it may be dried and mounted in xylol balsam. Sections should be dehydrated by soaking in absolute alcohol, then passed through bergamot or clove oil and mounted in xylol balsam. In all cases a ground, or contrast, stain of methylene blue or iodine green may be superimposed by steeping the preparation in a dilute aqueous solution of the dye, after the acid has been washed out; or Gabbett's acid-blue solution may be used in place of the nitric acid and separate ground stain.

Thus prepared, the leprosy bacilli are seen as bright red beaded rods; all other bacilli (except those of tubercle), if any be present, and the elements of the tissue, having lost the red colour through the action of the acid.

It has been found that bacilli which have been in alcohol take the stain better than those which are treated directly.

Leprosy bacilli are very resistant. Köbner found them in a fragment of tissue which he had left forgotten in a piece of paper for ten years. In Trinidad they were found in the remains of a nodule which had been inserted beneath the skin of a fowl two years before. The bacilli still took the characteristic stain, though the nodule was reduced to caseous detritus. Leloir had a similar experience with nodules which had remained two years and a half in the peritoneal cavities of guinea-pigs. He also dried a piece for twelve days in a stove, and on making sections found numerous bacilli which took Ehrlich's stain.

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[1] As this club-shaped formation cannot be detected in my own specimens, it may be suggested that the appearances shown in Mr. Pringle's photographs may be due to some of the rather short bacilli lying not quite flat in the field, or with both ends in focus at the same moment.

[2] Ehrlich's solution is also efficacious.

As has been truly remarked by Arning, we cannot at present say with certainty, by our histological methods, whether leprosy bacilli under examination be alive or dead.

By a special mode of preparation of the tissue, Unna came to the conclusion that the bacilli of leprosy are never contained in cells; but Dr. Rake and myself, and other observers (Thin, Hansen, etc.), are satisfied that cells containing their proper nuclei, and also bacilli in their cell substance, can easily be demonstrated by double staining.

Whether the bacilli, in addition to being within the cells, may also be free in the intercellular substance, and among the elements of the tissue, is not an easy question to decide. In whatever way the specimens are prepared, as sections or as cover-glass films, a number of cells must be injured or broken up by the process, and their contained bacilli set free. Moreover, a lepra cell may disintegrate in the course of nature, and leave a group of bacilli in its place. It is also probable that the secretions from the bacilli have a directly poisonous effect on the tissue elements in the neighbourhood, and, setting up inflammation, cause an accumulation of leucocytes. The latter may then, like phagocytes, take up bacilli, become enlarged—with multiplication of the contained bacilli—and ultimately suffer disintegration of the nucleus and alteration of the cell substance, and finally be represented by detritus and bacilli which have meanwhile multiplied. At any rate, although we have no evidence that they can live and multiply in the human body outside of the lepra cells, bacilli apparently free are often observed in the tissues.

If it be true that the bacilli can only live within cells, and not free in the fluids of the body, we may have in this fact an explanation of the chronicity of the disease, and of the difficulty of its communication.

In old nodules and in affected organs, brown masses or "globi" (Neisser) are often seen. These are dense collections of bacilli, more or less broken up into granules.

Distribution within the Body.—The leprosy bacillus is by no means evenly distributed throughout the body—it may be found in any viscus or tissue, or even in all (Cornil and Babes), but far more commonly in some than in others. In the trophoneurotic cases it is exceedingly rare, except in certain nerves. Hansen and Köbner have described them as occurring in the blood, and Leloir found them in that fluid in one case out of five examined. In no case in Trinidad have they been found in the blood, although observations were made during the acute outbreaks;

and this has hitherto been the experience of most other observers with blood drawn uncontaminated by leprous skin or bacilli-bearing tissues. Hansen figures them in leucocytes within blood-vessels, and in the endothelium of the latter. They have been found in the fluid of blisters raised over cutaneous nodules, but not in blisters over anæsthetic patches. The juice expressed from a leprous nodule contains them in abundance, as does the purulent discharge from the ulcerated nodules. In a few cases only have they been seen in the discharge from ulcers of anæsthetic lepers.

When there is leprous ulceration of the mouth, nose or pharynx, the bacilli are found in the patient's saliva. They have also been seen by Babes and Kalindero in vaginal mucus; but the Indian Leprosy Commission, who made a few observations on the point, were not successful in here finding them.

The sputum of cases in which the larynx is affected may contain them in considerable quantity. In one instance they were found by the Commission in the fæces of a leper in whose saliva they had previously been demonstrated.

They have not yet been seen in urine or in menstrual discharge.

The tissue in which the bacilli are found in the greatest profusion is undoubtedly the corium of the skin. When the leprous growth is fully developed, sections stained for bacilli may show masses of the latter so closely approximated that but little else can be seen in the field.

The bacilli have been found in the rete mucosum between the cells of the palisade and other layers, and they have also been demonstrated in the hair follicles. They have not been demonstrated by Dr. Rake or myself in the cutaneous anæsthetic patches of the trophoneurotic cases, nor has either of us seen them in the maculæ or erythematous patches of early leprosy; Hansen, however, appears to have found them with ease, especially in the recent spots. In the nerves of the anæsthetic cases as well as of advanced cases of dermal leprosy—wherever the nerve enlargements exist—the bacilli are found throughout the neoplasm, within the cells in the sheaths, between the nerve fibres, and also apparently free. They are said to be less numerous in the nerves of the purely trophoneurotic cases than in those of the "mixed" cases. In very old or arrested cases of the former, in which the nerve-trunk has become atrophied, the fibres degenerated, and the leprous cells disintegrated, the bacilli may be very few or altogether absent.

They are often found in the femoral lymphatic glands, especially in old-standing nodular or "mixed" cases.

The distribution of leprosy bacilli in other organs of the body and in the viscera seems to follow no general law. In the Trinidad autopsies mentioned above, the liver, spleen and testes were most commonly invaded. In the liver the bacilli are found in the new connective tissue which has been formed between the lobules, as well as in the lobule itself, among the hepatic cells; and they have also been described as occurring within the cell substance of the latter, in the lymphatic spaces, and in the small branches of the portal vein. In the spleen they are seen in the splenic cells as well as between them, and in the testis the bacilli are found principally in the increased connective tissue around the tubules, and occasionally within the tubuli seminiferi themselves, and in the epididymis.

The bacilli are much less commonly found in the kidney—of 77 kidneys examined at Trinidad, they were present only in 7—in the glomeruli, and in the endothelium of the renal vessels.

Among other organs in which they have been found are the ovary (Arning), the intestinal wall, the mesenteric and lumbar glands, in bone marrow and Haversian canals (Delepine and Slater), and in striped muscle-perimysium, endomysium and fibre. Chassiotis has described leprosy bacilli in the brain, but they were never seen at Trinidad either in the brain or spinal cord, although frequently sought; in one case they existed in the superior cervical ganglion of the sympathetic.

In the lungs undoubted leprosy bacilli must be very rare. Bonomé and Arning have described them, but they were never seen in the Trinidad autopsies. On the other hand, as we have seen, pulmonary phthisis is common among lepers, and in such cases the bacilli of tuberculosis are abundant in the pulmonary tubercles and in the sputum. Damaschino has found the bacilli of both leprosy and tuberculosis in the lungs of a leper. I have demonstrated leprosy bacilli in abundance in the trachea of a patient who died recently with extreme leprous stenosis of the glottis.

Distribution outside the Body.—Very little is known concerning the distribution of the leprosy bacilli outside the human body. Kaurin, after numerous experiments, failed to find the bacillus in the earth, or in the dust and air of the rooms inhabited by lepers. In Trinidad, examination of the soil of graves of lepers showed none of the bacilli; and observations made on salt fish, salt pork, etc., in the asylum were negative. At the Almora Asylum the Leprosy Commissioners prepared 100 cover-glasses from earth taken from the banks and paths on which the lepers were in the habit of sitting and walking. In 7 of the cover-glasses only were bacilli found, to the number of 10 altogether. At the Tarn Taran Asylum 450 similar specimens were prepared, but no bacilli were found. Water from tanks at Bombay and Tarn Taran in which lepers bathe also gave negative results, although they could be easily detected in basins of water in which leprous ulcers had been washed. A large number of examinations of fish, dried and fresh, in Burma, Bombay, and Darjeeling, also failed to show the bacilli. Flies and mosquitoes were allowed to feed on discharges from ulcers and on leper's blood, and were afterwards examined for bacilli, but with no positive result.

Cultivation Experiments.—Since its discovery numberless attempts have been made by pathologists to cultivate the bacillus outside the body, but up to the present time without undoubted success.

Hansen kept leprous blood in a moist chamber, and obtained a mycelial growth, which, as he afterwards admitted, had nothing to do with the leprosy bacillus. Neisser inoculated blood serum with fragments of leprous tissue, and kept pus and juice from nodules in sealed capillary tubes. From these experiments he described three different bacilli, which, however, he failed to cultivate in generations. Arning, in Hawaii, allowed pieces of leprous tissue to macerate in water, and observed a multiplication of the bacilli, as also in the tissues of a deceased leper who had been buried for three months.

These observations were repeated at Trinidad without positive result, and numerous experiments were made with various media—including blood serum, ascitic and hydrocele fluid from lepers, and combinations of them with agar, glycerine jelly, etc. Growths of micrococci were frequently obtained, but never leprosy bacilli. In 1887 Bordoni-Uffredussi announced that he had been successful. He had placed portions of bone marrow, in which he had found free bacilli, in peptonic-glycerine-serum, and obtained cultures of a small bacillus, often bulbous at the ends and resembling those found in the tissues, but retaining the fuchsin stain with more difficulty. Inoculations of animals with the cultivated bacilli were negative. Giantusco subsequently obtained a cultivation which Bordoni-Uffredussi considered identical with his own, and Campana has more recently described a third bacillus cultivated from leprous material. A careful examination of specimens from all these cultures is not convincing.

Culture experiments were carried out in India by the members of the Leprosy Commission, who also thought at first that they had been successful. In one series of observations sterilised capillary tubes containing blister fluid from healthy skin were inoculated with fluid from blisters over leprous nodules. The tubes were carried about in the axilla for a month, and bacilli somewhat resembling those of leprosy were then found in them. Subcultures in glycerine-bouillon gave a growth of bacilli, which retained a pink stain after treatment with Ziehl's solution and dilute nitric acid, but the bacilli were shorter and thicker than those obtained from the leprous tissues. Further subcultures resisted the action of the acid still less. Inoculations in animals were without effect.

I have myself employed a medium containing broth made from the tissues of a leper with peptone, glycerine and agar. A growth seemed to take place at first, but afterwards disappeared, and attempts at subcultures proved futile.

The remarkable difficulty of cultivating the bacillus of leprosy contrasts strongly with the ease with which the bacillus of tuberculosis can be grown outside the body, and forms indeed an important distinction from it.

Inoculation of Animals.—An enormous number of attempts have been made to introduce the leprosy bacillus into the bodies of animals, but in very few instances has there been any spread or multiplication of the organisms beyond the immediate neighbourhood of the inoculation. Neisser inserted a piece of leprous tissue beneath the skin of a dog, and subsequently found a growth of bacilli at the site of the inoculation. Damsch and Vossius introduced portions of a nodule into the anterior chamber of rabbits' eyes, and described infiltration of the iris, ciliary body and Descemet's membrane with cells containing leprosy bacilli, but similar results have been obtained by Wesener, Leloir and Campana, by implanting leprous material which had been for years kept in alcohol. Campana inoculated the vascular combs and wattles of fowls, and often obtained a local inflammatory swelling containing large cells which had taken up the bacilli in the manner of phagocytes. Köbner and Hansen failed to infect monkeys, and Hilliaret and Gauche a pig. Vidal also inoculated a pig, and a year afterwards he found bacilli in the remains of the implanted mass, but none in the surrounding tissues.

Arning, Kaurin, Leloir, and Thin have hitherto been unable to establish leprosy in animals, and the Trinidad experience has been the same. During the last ten years attempts have been made with guinea-pigs, rabbits, cats, pigs, bats, fowls, small birds, a dog and a parrot. Pigs and fowls were also fed at the asylum for long periods—some as long as two years—with cutaneous nodules and pieces of viscera from lepers, but no results were obtained.

On the other hand, Melcher and Ortmann, four months after inserting pieces of fresh nodule in the eyes of rabbits, found the cæcum, spleen, lungs, and lymphatic glands infiltrated with growths containing bacilli, which he regarded as those of leprosy. This opinion was confirmed by Arning and Ruffer, but Wesener, who repeated the experiments, came to the conclusion that no proliferation of the bacilli had occurred, but merely a diffusion of those introduced. He and Huppe believe that Melcher and Ortmann, like many others, have sown leprosy and reaped tuberculosis.

Tedeschi inoculated a monkey in the spinal dura mater. Death occurred in eight days, and bacilli resembling those of leprosy were found in the new tissue at the site of the inoculation, and in the cerebro-spinal fluid and spleen. In this case, too, it is probable that a diffusion, without proliferation, of the bacilli had taken place.

The evidence given above, though to some extent conflicting, may on the whole be regarded as supporting the view expressed by Besnier—that leprosy is strictly a human disease which cannot be transmitted to animals.

Inoculation in the Human Subject.—A considerable number of persons have from time to time allowed themselves to be inoculated with leprous material in order to test whether the disease could be so communicated, but as yet with no positive results. Danielssen, Bargilli, Holst and Tilsch made such attempts, but always with a negative result. Profeta inoculated himself and nine other people, and sixteen years afterwards there had been no evidence of the disease in any of them. Hansen introduced material from nodular cases into anæsthetic cases, but with no development of nodules in the latter, and similar experiments were made at Trinidad with thirty-three anæsthetic lepers—nodulation appeared only in one of them four years after the inoculation. We have, however, already seen that after some years dermal nodules may spontaneously appear in such cases. On the other hand, Arning inoculated an apparently healthy convict at Honolulu, and three years later the man manifested leprosy. This case has been regarded as conclusive, but it has since been found that several members of his family—a son, nephew and maternal cousin—have also become lepers in the ordinary way. Indeed, for an experiment of the kind to be absolutely conclusive, it should be made in a country where leprosy is not endemic, and on a subject who could never have been in contact with the disease.

It cannot, therefore, be admitted that the intentional inoculation of the leprosy bacillus in the human subject has hitherto been successful.

Etiology.—We have seen in the foregoing pages that leprosy is always associated with a specific bacillus, and it has also been shown that this bacillus has never yet been certainly cultivated outside the body, or undoubtedly inoculated, with subsequent proliferation, into the tissues of man and other animals.

Although it is thus evident that in the case of leprosy only the first of Koch's postulates is as yet fulfilled, nevertheless from the close analogy between the bacilli of leprosy and of tuberculosis, and from other considerations, pathologists have felt justified in accepting the bacillus lepræ, or the poison secreted by that organism, as the true cause of the malady. This being granted, we must regard leprosy as a "specific infective disease," and admit the possibility of its communicability from one person to another. Moreover, as the bacillus has never yet been found growing outside of the human body, although it is thrown off in great quantities in leprous discharges, we are driven to acknowledge that its only source at present known is in the bodies of lepers.

In discussing the principal ætiological factors which have been ascribed to the disease, we shall see that the question is a difficult one, and that, in the present state of our knowledge, no decided conclusions can be arrived at. We shall briefly inquire to what extent practical experience confirms the above considerations.

Contagion.—Historical Evidence.—It has been argued that history has proved the contagiousness of leprosy, and that in remote times it must have been spread in that way from Egypt to the Levant, Greece, Italy, and the rest of Europe. The absence of early record of it in a country does not prove that the disease did not exist there; but we may assume that the diffusion of knowledge from the East would tend to the observation and recognition of such a disease. Moreover, other possible etiological factors which obtain at the present day must have been existent then, and, as we shall see, it is by no means improbable that the virus of the disease may gain an entrance into the human system in more ways than one.

It has been further maintained that the contagiousness of leprosy is proved by the diminution or extinction of the disease after the segregation of lepers in the Middle Ages in England and other parts of Europe. We know, however, that the isolation of lepers was never absolute; and that although they may have had to appear in a special dress and with a pair of clappers, and were objects of abhorrence, they were frequently allowed, nevertheless, to wander about and shed their bacilli over the surface of the earth. It is needless to say that antiseptic precautions were then unknown. We may indeed conclude that historical evidence, although indicative of some amount of human transmission of the disease, does not prove its communicability only by contagion.

Contagion at the Present Day.—Most of the alleged instances of communication of leprosy from one person to another have occurred in countries where the disease is endemic, and are therefore open to the objection that the virus may have been acquired otherwise than by contagion. Even in such countries instances of apparent contagion, with full data, are comparatively uncommon. For instance, during the stay of the Leprosy Commission in India, eight cases of the kind were brought forward, but only one stood the test of close examination. This case was that of a sweeper in the Calicut Asylum, in whom leprosy appeared after dressing the sores of the inmates for twenty years. At Trinidad, in ten years, only one case was noticed of apparent contagion—that of a man who developed the disease two years after living with a leprous woman. Many cases, however, have been recorded in India, British Guiana, and other parts of the world; and Hillis reports 60 cases of leprosy contracted by healthy persons living in the immediate vicinity of the Mahaica Asylum. Donovan has recorded a case from the Lepers' Home, at Spanish Town, Jamaica. The cook employed there for seventeen years has recently exhibited the disease. He frequently slept at the asylum, and was assisted in his work by two leper inmates. No member of his family had ever been affected. Supposed instances of contagion have also been brought forward within recent years by Moore and Cayley in India, Ross in South Africa, Heidenstam in Cyprus, Münch in South Russia, Simons in South Africa, Taché in New Brunswick, Hellat in the Baltic Provinces, and Azevido Lima in Brazil; some of these cases were of attendants and others in leper asylums.

The accounts of Europeans who have contracted leprosy in leprous countries are far more important, for they are less dirty and careless in their habits, and cannot, like some natives, be regarded as having any special tendency to take the disease. Several instances are on record of Europeans who were associated with lepers having acquired the malady, for example, Father Damien in Molokai, Father Boglioli in New Orleans, a French Sister of Mercy in French Guiana, and another in Tahiti. The two latter are said to have pricked their fingers with needles while sewing lepers' clothes. Small isolated outbreaks, traceable to the settling of lepers in districts previously free from leprosy, have also been reported in Russia, Louisiana, New Brunswick, Cape Breton, and Parcent in Spain.

On the other hand there is a mass of negative evidence. Thus the

Dominican Nursing Sisters in the Trinidad Asylum have been in constant contact with the lepers for twenty-six years, and not one of them has become infected. The experience in a large number of other asylums has been the same. Zambaco Pacha relates the case of the resident priest at the asylum at Constantinople, whose family for three generations have lived among and freely mixed with the lepers, without contracting the disease; and similar instances are indeed innumerable. Medical men in various parts of the world have pricked their hands in surgical and post-mortem operations on lepers, and have not taken the disease. Many accounts have been published of healthy persons cohabiting with lepers for years with impunity. Three cases in point are, or have been recently, under my own observation in England. Leprosy has not yet spread from the Chinese in California, nor from the Norwegian lepers who emigrated to North America; and although there is always in London, Paris and other European centres an appreciable number of patients who have contracted leprosy abroad, the disease, with the exception of the cases about to be referred to, has not been acquired by people with whom the lepers have associated.

Instances of Transmission in Leprosy-free Countries.—The most important case of this kind yet known is that recorded by Hawtry Benson in Dublin. An Irish soldier returned from India with fully-developed leprosy. For a year and a half his brother slept in the same bed with him, and he wore the leper's clothes after the latter's death. Three years later this brother, who had never been out of the United Kingdom, manifested leprosy and died of it. The diagnosis was confirmed by medical men well acquainted with the malady, and we may accept the case as conclusive. Similar instances, perhaps not quite so free from doubt, have been also recorded by Liveing, Rees, and Atkinson.

We must therefore, on the whole, admit that in some cases leprosy has been communicated from one person to another. Possibly such instances would be brought before us in greater numbers were it not that the disease is one of very slow incubation, and its prodroma are frequently slight and overlooked. Even with diseases of acknowledged contagiousness and obvious early symptoms, it is often difficult to trace the contagion. But if leprosy be "contagious" in the ordinary sense of the term, it must be so in a comparatively very slight degree, far less so indeed than tuberculosis. We have seen how difficult it is, to say the least, to inoculate the disease, and we have no evidence that the bacilli can enter the body through the unbroken skin. When it spreads, therefore, as it has done in certain countries to a significant extent within a few years, we are justified in asking whether there must not be something more than mere contagion to account for its increase.

Vaccination as an alleged Ætiological Feature.—Certain persons blindly prejudiced against the practice of vaccination have sought to lay the spread of leprosy to its charge. For many years the minds of observers, competent and otherwise, all over the world have been open to the possibility of the introduction of the disease with the virus of vaccinia, and it is remarkable how few authentic instances have been brought forward of such supposed dissemination.

Dr. Gairdner has recorded a case in which a doctor in a tropical island vaccinated his own child from a native child in whose family leprosy existed. It was stated, though not proved, that the vaccinifer afterwards became a leper. The child of a Scotch sea-captain was vaccinated with lymph taken from the doctor's infant, and in both these children leprosy subsequently appeared; they were seen in Scotland by Gairdner, who believed that the disease had been transmitted by vaccination.

Daubler at the Cape of Good Hope, Chew in Calcutta, and Hillis in Demerara, as well as Erasmus Wilson, Ranald Martin, Swift, and Piffard, have also published cases in which it was suspected that the disease had been so acquired; but as all the instances occurred in countries where leprosy was prevalent, and where the disease might have been acquired by other channels, they cannot be regarded as free from doubt. The accounts of many of them, moreover, are extremely vague, and give by no means the whole of the facts.

Perhaps the strongest evidence connecting vaccination with the dissemination of leprosy comes from Hawaii, where, as Arning has pointed out, local accumulations of fresh cases were observed shortly after universal arm-to-arm vaccination had been carelessly performed; but, as that observer remarks, the coincidence may be explained in other ways, such as the multiplicity of infective foci by migrations of lepers, use of contaminated food, introduction of the plague of mosquitoes, etc.

The risk of vaccination, if any, must be very small, for the following reasons:—

In the first place, numerous experiments in this direction have proved that vaccine lymph obtained from lepers is as a rule free from leprous bacilli, especially when the vaccination has been performed on unaffected areas of skin. In 27 specimens of such lymph examined in Trinidad none were seen, and in 93 examined at Almora by three members of the Indian Commission, bacilli—and these were doubtful—were only found in one case in vesicles produced over a nodule, and in another in vesicles formed on an anæsthetic patch. Simpson, however, in Calcutta, described bacilli in vaccine lymph from lepers, and Arning observed them in lymph obtained from a vaccinated leper of the nodular form, but none in an anæsthetic case.

Secondly, in leprous countries bovine lymph is and has been for many years extensively used, or, at any rate, human lymph imported from non-leprous countries, and certainly not from vaccinifers tainted with leprosy.

Thirdly, in those rare instances in which lymph has been imported from places where leprosy was prevalent, and used in districts comparatively free from the disease, we might expect, were there any causal connection between vaccination and leprosy, that the number of cases in the latter districts would, in the course of time, be numerically increased. Between the years 1867 and 1884, Surg.-Major Pringle superintended the vaccination of at least 2,000,000 persons in the plains between the rivers Ganges and Jumna—a district where leprosy was not particularly common—with lymph obtained in Ghurwal, where the disease was extremely prevalent, but nevertheless the recent census returns have shown no increase of leprosy in the former district.

Fourthly, in most countries where leprosy has been steadily diminishing, the practice of vaccination has been coming more and more into vogue, as, for instance, in Norway, Finland, Jamaica, and many parts of India, etc.

Fifthly, the vast majority of lepers throughout the world—for example, in India at least 78 per cent—have never been vaccinated at all.

Heredity.—Until recently a belief in the heredity of leprosy was widely spread among medical men, as it still is among the ordinary inhabitants of infected countries; and it was often pointed out that the disease seemed to prevail in certain families. In such cases, however, the affection appeared in collateral members rather than in the direct line.

Even if it be true, as suggested by Virchow, that an inherited disposition to the disease may exist in certain families (and there is reason to doubt whether such a predisposition be transmitted to any large extent), a close investigation of the facts indicates that heredity can have but little effect in the dissemination and perpetuation of leprosy.

The following considerations bear upon this question:—

(1) In all the leprous countries of the world a genealogical family taint can be traced in comparatively few cases; and even those in which brothers or sisters and collateral branches are or have been affected are not so general as might be supposed. Thus, in India, the Commission could only discover family histories of the disease in 5 or 6 per cent of the lepers seen; and in Crete, Vandyke Carter found a similarly small proportion of "hereditary" cases. Among 118 patients at the Tarn Taran Asylum, 38 stated that one or more of their blood relations were or had been lepers; but of these, in only 16 had one or both of the parents or grandparents been affected. It is, moreover, not stated whether the disease made its appearance in the latter before or after its development in their offspring.

(2) Immigrants from leprosy-free countries, or their immediate descendants, in whom there could be no hereditary trace of the disease, frequently become leprous in infected countries.

Of 42 cases of leprosy recorded by Blanc at New Orleans, 12 were natives of foreign countries (7 German, 1 Austrian, 1 English, 1 Irish, 1 French, and 1 Italian), and of the remainder, 18 were the children of foreign-born parents (chiefly German and Irish), "from which we conclude," he says, "that if the disease be hereditary it must be derived from a variety of foreign sources, and, if acquired, then it seems to attack the children of immigrants as often as those of the older native families."

(3) One or more of the younger generation often become lepers, while the parents and grandparents are not affected; and these latter occasionally become diseased some time after the children.

(4) When lepers beget children the latter frequently remain free from the disease; for instance, in the Almora Orphanage, where they are separated from their mothers at an early age, only one out of fifteen has manifested leprosy; in the Trinidad Asylum Orphanage, however, one in eight became affected.

Bibb, on the other hand, reports two cases in Mexico in which the subjects were removed at birth from leprous mothers, brought up in districts free from leprosy, amid healthy surroundings, and never in contact with lepers, but who nevertheless became diseased at or after twenty years of age. He regards these as good instances of hereditary transmission.

Perhaps the strongest evidence yet adduced against the heredity of leprosy is that brought forward by Hansen, who made a special journey to North America to discover what had become of the 160 known Norwegian lepers who had emigrated and established themselves in the States of Wisconsin, Minnesota, and Dakota. He found that not one of their descendants, as far as the great-grandchildren, had exhibited the disease.

(5) Lepers are extremely sterile; indeed, if left freely to marry, the disease, if its transmission depended only on heredity, would soon become extinct. At Molokai, in eighteen years, of 2864 lepers who were incarcerated, but with free intercourse among themselves, not more than 26 children born in the settlement were found living at the end of the period, and of these only two had become lepers.

In India it has been calculated that the average number of children to each marriage between lepers, or between a leper and a healthy person, is less than one.

At Tarn Taran 21 children were the progeny of 55 marriages. Only four females in that asylum in whom the disease had already declared itself gave birth to children, and these amounted to five.

Two lepers, a male and female, under my care in England have had children since their disease appeared—the man four, and the woman two. In both families the children have remained perfectly healthy, as well as the wife of the one and the husband of the other.

(6) Congenital cases of leprosy are very rare; of the few instances recorded in which infants were born with supposed marks of the disease upon them, it is quite possible that the symptoms were really those of syphilis. Navarro has reported two cases in Colombia as occurring in 1847 and 1848, and two infants at Trondhjem are reported to have been leprous at or shortly after birth. Although children are sometimes affected, the enormous majority of the cases show the typical period of onset of the disease to be in young adult life; some few lepers, however, do not present the first signs of leprosy until extreme old age. I myself saw in Norway three patients upwards of eighty years of age, who had been leprous for two or three years only.

Influence of Diet.—At various times and in various countries a great many articles of food have been declared to be the cause of leprosy; but although it is quite possible that the bacilli may sometimes gain entrance to the body with the ingesta, and that the tissues of those who partake of certain foods may be rendered less resistant or more susceptible to the growth of the micro-organism, we cannot, on the facts before us, reasonably connect the disease with any particular diet.

A causal relation has been alleged between leprosy and a vegetable diet, a diet of salted food, of food without salt (ably argued by Munro), of pork, of fish, and of many other things, and the use of contaminated water has been suggested by Liveing and others. The fish theory, which dates back from the time of Avicenna, has been supported by various writers, and in recent years particularly by Mr. Hutchinson. It is argued that the chief centres of leprosy are on the sea-coasts, or along the borders of large rivers, where the people live chiefly on fish—often more or less decomposed, uncooked, dried or salted; but it can be shown that the disease is also largely prevalent in places far from seas and rivers, and where fish cannot be obtained, for example, in the mountains of Kurdistan, many parts of India, Kashmir, and so forth. In India certain castes of Jains, Brahmins and Banias religiously abstain from all animal food, and many of them at least never taste fish; nevertheless leprosy occurs amongst them. In the hill districts of Almora and Dehra Dun the Commissioners met with lepers who not only had never eaten fish, but who did not even recognise the form of a fish.

Fish and preparations of fish of all kinds have been carefully examined for bacilli in leprous countries, but without success.

The Influence of Poverty, etc.—That poverty and bad hygiene have an indirect effect on the prevalence of leprosy must, however, be freely admitted. The poor in all the countries in which the disease is endemic suffer more frequently than the rich, although the latter by no means escape; and we may well believe that insufficient or innutritious diet may render people more prone to its acquisition. It is thought by many, indeed, that the diminution and extinction of leprosy in most of the countries of Europe was due more to the improved well-being of the people as to food, clothing, cleanliness, etc., than to the measures of isolation.

The Influences of Race, Climate, etc., need be very briefly alluded to. No nations are exempt, and the disease may occur in the coldest as well as in the hottest climates, in moist or in dry districts, in plains or on mountains. Nor has any direct connection been shown between leprosy and such other diseases as syphilis, tuberculosis, scabies, etc. With leprosy, as with other diseases, anything which lowers vitality may render the system more liable to its acquisition and less able to resist its progress; and it is also possible that any breach of the skin may facilitate the introduction of the virus. In this latter way, possibly, the bites of insects, scabies, and other affections of the kind may have an indirect influence, although this has not been proved.

We know by definite experimental proof and by clinical observation that tuberculosis—the first cousin of the disease under consideration—may be introduced into the body by more than one channel, and we may suppose that leprosy likewise may be acquired in several ways—by paths of entry which have not as yet been fully traced.

The Diagnosis of Leprosy.—When nodular leprosy is fully developed its diagnosis should be a matter of no difficulty ; for apart from the obvious naked-eye appearances—the localised nodulations and thickenings, the history of the primary eruptions, etc.—a small piece of new growth excised or scraped will always exhibit the specific bacilli. In an early stage the eruption might be mistaken for a syphilide, but a microscopical examination may settle the matter, or the test of anti-syphilitic treatment may be tried. The characters of the primary eruption already described, its special sites of predilection, its far more chronic course, and the accompanying local loss of hair, also distinguish the leprous from the syphilitic exanthema. It must not be forgotten that syphilis may coexist with leprosy ; its characteristic lesions should therefore be looked for.

Certain cases of tuberculides — Lupus vulgaris, L. erythematosus, scrofulodermia, etc.—have at times been mistaken for leprosy ; but the history, previous discolorations, and other characteristics should suffice to distinguish the diseases, even without an examination for the bacilli. The same also may be said of the idiopathic erythemata which may resemble the first stage of the leprous eruption, especially of erythema exudativum, in which, however, the papules are smaller, run a more acute course, clear up from the centre as they increase in size, and leave but a transitory stain ; there is, moreover, no alteration of sensation or febrile disturbance.

Many other diseases causing tumefactions of the skin have from time to time been mistaken for nodular leprosy—for instance, pigmented sarcoma and other malignant growths, elephantiasis arabum, molluscum fibrosum, yaws, acne, etc.—but attention to the above descriptions should leave no doubt in the mind of the observer.

On the other hand, it is not always so easy to distinguish cases of purely neural leprosy from certain other affections in which the nervous system may be implicated. Well-advanced cases have frequently been confounded with syringomyelia, Morvan's analgesic whitlow, progressive muscular atrophy, peripheral neuritis, sclerodactily, ainhum, and Raynaud's disease. The resemblance of these diseases to certain cases of this form of leprosy is, indeed, so great that Zambaco Pacha has unhesitatingly affirmed that they are all of them, as well as sclerodermia and morphœa, modified or attenuated forms of leprosy. As a general rule, however, the sufferer from neural leprosy exhibits at some stage the characteristic, discoloured, and anæsthetic patches on the skin, and has been in leprous districts or associated with lepers. Moreover, the bacillus may be found sooner or later in the neoplasm in the nerves.

The eruption in the early stages may sometimes closely simulate leucodermia ; and in children especially, or in patients of weak intellect, the diagnosis may be retarded by the difficulty of determining degrees of anæsthesia.

It has been estimated that at least 5 per cent of the supposed lepers in the East are suffering from other diseases superficially resembling true leprosy.

Prognosis.—The prognosis in leprosy is very bad. It has been said "once a leper always a leper," and that the disease is incurable. It is true that with very few exceptions the malady goes on from bad to worse in spite of all treatment, and that the patient's life is shortened. Yet it must be remembered that in many asylums in Norway, and elsewhere, there are inmates in whom the disease has been arrested for many years—the cases practically cured, but of course with more or less deformity and loss of tissue.

Several instances of apparent cure have been recorded by Munro, Hutchinson, Cottle, Unna, Phillippo, G. Fox, Francis, the Norwegian physicians, and others, and in some of them, at any rate, a recrudescence of the disease had not appeared up to the time of the death of the patient in old age. The official report for Norway gives the number of cured cases at thirty-eight during the five years 1881 to 1885. There is, indeed, reason to believe that there is hope in some cases, especially if measures be adopted at an early stage. The disease occasionally proves fatal in a year or two, or it may progress more slowly, especially when only the nerves are affected, for several decades; lepers are occasionally seen in whom the disease has been slowly progressing for forty years. Observations at Trinidad gave in 18 years an average duration of life of 6½ years for the nodular, 10 years for the neural, and 9¾ years for the "mixed" cases. These figures seem worse than those given by Danielssen and Boeck—namely, 9½ years in the nodular, and 18½ in the neural form; but those observers excluded all deaths from intercurrent diseases. Carter's calculations for Bombay approximate to the Norwegian statistics; and Leloir gives 8 to 12 years for nodular cases, and 18 to 20 for the neural. When the affection makes its appearance in early life, its course, especially in the neural form, is usually more rapid than when it attacks old people; and frequent acute outbreaks of nodules, and early implication of the larynx, make the prognosis more unfavourable. The progress of the disease is usually slower in cases with diffuse infiltrations of the skin than in those in which crops of discrete nodules frequently appear. The presence of visceral complications shortens the expectation of life in all cases of leprosy.

The Treatment of leprosy is by no means satisfactory; but although an absolute cure can rarely be anticipated, it is a mistake to suppose that nothing can be done to prolong life, or to mitigate suffering in the unfortunate victims.

We may consider the treatment under the heads "Hygienic," "Medicinal," and "Surgical."

Hygienic.—It is of the utmost importance to lepers, as to other invalids, that their surroundings should be healthy. They should have plenty of fresh air, their dwellings be well ventilated and dry, the extremes of heat and cold avoided, strict cleanliness enforced, and good, nourishing diet provided, such as fresh meat and vegetables, with no salted or indigestible food. Fish and other decomposable substances should not be eaten unless quite fresh. Some few lepers have stated that their ulcers have become worse after eating fish; but this is by no means the general experience. Plenty of exercise should be taken, as well to promote the general nutrition as in order, if possible, to excite the action of the sweat glands. The patients should be warmly clothed, for they are usually very susceptible to cold; and we have seen how liable they are to disease of the kidneys.

Removal to another climate, especially to a country in which the disease is not endemic, often has a very beneficial effect, particularly in the early stages of the disease. Many colonials, for instance, who have come to uninfected parts of Europe have probably lived longer than they would have done in their own countries.

Medicinal.—No specific drug has yet been discovered for leprosy, although it must be admitted that effects, both locally and generally beneficial, can often be produced by certain external and internal remedies. In estimating their value in individual cases, however, it must not be forgotten that the symptoms of the disease are sometimes ameliorated, or even arrested for a considerable time, spontaneously or by improved hygienic conditions alone.

Of the numerous vegetable oils which have been used for leprosy, oleum gynocardiæ, or "chaulmoogra oil," appears to be the most efficacious, and it is certainly believed in by the lepers themselves. At the Trinidad Asylum, in eighteen cases in which its prolonged use was tried, the chief effects observed were—(1) Increase of perspiration, (2) decrease of the nodules, (3) improved appetite, (4) lessening of anæsthesia, (5) greater suppleness of the skin, (6) lessening of the pains in the joints.

The oil may be given in doses of 10 minims, preferably in capsules, two or three times a day, and gradually increased until one or two drachms are taken in the twenty-four hours. At the same time it should be well rubbed in—either pure or as an emulsion with an equal part of lime water—twice a day over the affected parts of the skin, or even over the whole body. The active principle of the oil, gynocardic acid, has also been prescribed internally by Besnier and others. The soda and magnesium salts are well borne, and in at least two cases in England under my own care they have appeared, in combination with external treatment, to be of distinct benefit.

Gurjon oil, which is used internally and externally in the same doses and manner as the chaulmoogra, has not seemed at Trinidad to be so useful. It is possible that the good results originally obtained by Dougall in the Andaman Islands were in part due to the fact that the patients, being convicts, were compelled to inunct themselves in a most thorough manner twice a day for two hours each time. Hillis speaks well of the gurjon oil treatment.

Others have not been equally successful with these oils, and the failures may have been due to the difficulty of carrying out methods of treatment so prolonged, troublesome, and disagreeable. Phillippo of

Jamaica has brought forward a case of well-marked leprosy of six or seven years' duration, which he treated vigorously with gurjon oil externally and chaulmoogra internally from 1879 to 1886. The man during that time practically "lived" in grease. Improvement gradually set in after the first two years of the treatment, and at the end of the period all the symptoms had disappeared. He had remained "cured" for five years when the account was published in 1890.

It has been suggested that the persistent and thorough application of any oil may ameliorate leprosy; and good results have been especially claimed for the cowti oil advocated by Bhao Daji of Bombay. The latter oil has not, however, proved so useful as chaulmoogra in the experience of other physicians.

The Beauperthuy treatment, which has been much lauded, consisted in applying cashew-nut oil, as a local caustic, to the nodules and patches, prescribing at the same time careful diet, attention to the functions of the skin by frequent friction and baths, and other hygienic measures, as well as internal medication with alkaline salts or perchloride of mercury. The cases which were reported as cured, however, subsequently relapsed. Mercury is of little or no therapeutic value in leprosy, except when complicated with syphilis.

In some cases at Trinidad arsenic was beneficial. It was administered as the liquor arsenicalis, commencing with three minims and gradually increasing the dose until the limit of toleration was reached. In two cases there was a marked diminution of the febrile nodular exacerbations. This drug has also been employed in leprosy by Mr. Hutchinson and others.

The supposed specific of the Chinese, "Hoang Nan," has proved of little or no use in Hawaii, India, etc.

Danielssen obtained better results in leprosy with salicylate of soda than with any other drug. When indicated he also gave cod liver oil, iron, quinine, etc.

Lutz reported good results from the exhibition of salol in large doses, 20 to 30 grains three times a day; and Cook in Madras also found a temporary mitigating effect from its use, but the latter came ultimately to the conclusion, after a three months' trial in twelve cases, that it has really no therapeutic value in leprosy.

The reducing remedies, ichthyol, resorcin, pyrogallol and chrysarobin, have been strongly recommended by Unna, who has published a case of supposed "cure" by their use. Many observers have, however, found that, although local improvement may be effected by these means, they have not justified expectations. A similar remark may be made in regard to europhen, which Goldschmidt found useful in one case in Madeira.

Potassium chlorate was recently given in large doses by Caneau to a leper in Guadaloupe, who took 675 grains in three days, with distinct diminution of the nodules. It was tried on two patients at the Trinidad Asylum in doses amounting to 80 to 100 grains a day for several weeks. Only slight decrease was noticed of the nodules, probably not more than could have been effected by free purging with magnesium salts.

The injection of tuberculin has been shown to be practically valueless in leprosy by a considerable number of observers including myself. Constitutional disturbance is as a rule produced, but of a somewhat different character from that caused in tuberculous patients, and some of the nodules may soften and disappear. Fresh ones, however, crop up, and the patients are generally no better off after the treatment than before.

I have administered thyroid gland to two patients in England, and in one the effect was apparently good; the man felt better in every way since taking the tabloids for about a year, and had no febrile attacks; there seemed also to be some lessening of the cutaneous induration. In Trinidad it was tried for a few weeks on five patients with well-developed nodular leprosy, with but little effect. In most of them the symptoms of thyroidism were produced.

The inoculation of erysipelas in one case has had a good result, but the treatment is dangerous, to say the least of it.

Experiments in connection with blood-serum therapy have been commenced at the Trinidad Asylum, in the anticipation that a specific antitoxine may be discovered for leprosy.

Surgical.—Surgery can do much for lepers; and operations, when indicated, may be performed upon them without hesitation. Their tissues indeed heal with rapidity, in consequence, it is believed, of the excess of fibrin factors which, as shown by Danielssen and Boeck, Hillairet and Rake, is contained in their blood. The mean percentage of fibrin obtained from leprous blood at Trinidad in fifty observations was found to be 0·76.

Amputation of a useless and encumbering member is sometimes advisable, especially in cases of gangrene. Nerve-stretching has frequently been of service in combating the intense pain which may result from the neuritis; indeed, the healing of perforating ulcers may be thus promoted, and improved sensation may follow the operation. Of 100 stretchings at the Trinidad Asylum more or less relief was experienced in forty-seven. M'Leod, Lawrie, Downes and others in India have employed nerve-stretching with much benefit; and M'Leod has also recommended "nerve-splitting." The best treatment for perforating ulcers of the sole was found at Trinidad to consist in passing a bistoury right through to the dorsum of the foot, and thence cutting or splitting all the tissues forward to a point between the toes; the wound is then allowed to granulate.

Dead bone should always be removed when practicable, and thus gangrene may often be arrested. Sinuses should be slit open, and ulcers freely incised down to the bone. Iodoform, carbolic acid, or other antiseptic substances and dressings should be used.

Cutaneous nodules may be freely excised, especially when they cause obstruction, as on the eyelids, prepuce, etc.; and according to some observers they do not return. Free incisions are often of service in relieving the hide-bound condition associated with leprous infiltration of the skin, and in obstructing the nutrition of the new growth.

When the new growth is invading the cornea, iridectomy, performed before the iris is infiltrated or adherent, may preserve some vision for a time; Boeckmann and Kaurin have found keratotomy sometimes of use in saving a cornea from a growth encroaching from the sclerotic. Trachelorrhaphy is also occasionally indicated for the paralytic ectropion.

Tracheotomy frequently prolongs life in leprosy; and there are lepers going about in the various asylums in Norway, etc., who have worn the tube for many years. When the larynx becomes invaded, and dyspnœa is threatened, the operation should be performed.

The Prophylaxis of Leprosy.—If we grant (1) that leprosy is due to the presence of a specific bacillus, (2) that the habitat of this organism is the human body, and (3) that the parasite may pass from one host to another, it follows that the most radical prophylactic measure against leprosy is the total avoidance of all contact with lepers, with anything that may come from their bodies, or with anything that they may touch. We have seen, however, that practically the contagiousness of leprosy, if it exist, is comparatively slight, that its inoculation is extremely difficult to bring about, and that it is a somewhat rare event for persons in association with lepers to contract the disease. Nevertheless, even though the risk be small, it should be borne in mind; and people who have to live in leprous countries, and who may sooner or later, knowingly or unknowingly, come under the influence of the contagium, such as it is, are well advised in avoiding close contiguity with lepers, in preventing the latter from handling food, utensils, clothing, etc., which the healthy have to use, and generally in adopting all common-sense sanitary precautions. Medical men and attendants particularly should be careful; and, if there be abrasions or cuts on their hands, should abstain until their wounds be healed from touching the lepers; at other times after tending their patients they should wash their hands with antiseptics.

Indeed, similar prophylactic measures may be taken as against tuberculosis and syphilis, although both of these diseases, it is needless to say, are far more readily communicable than leprosy.

The Question of Compulsory Segregation.—A great many sanitary authorities recommend the absolute isolation and segregation of all lepers; but although, theoretically, such a measure might be expected in time to eradicate the disease from an infected country, a number of valid arguments may be adduced to show that it is hardly practicable or even advisable in many places. It has been alleged over and over again that it was in consequence of the stringent laws of the Middle Ages that leprosy was stamped out in many places, and also that the isolation of lepers in Norway is causing the diminution of the disease in that country. That these attempts at isolation and segregation may have had something to do with such results need not be denied; it is practically admitted above that every leper may be regarded as a breeder and carrier of the bacilli, and thereby as a possible focus for the dissemination of the disease; but real isolation has never been complete, and is never likely to be. Even in the olden times it is well known that wealthy and powerful persons afflicted with leprosy managed to escape the pains and penalties and to avoid incarceration, and there must have been many of all classes secreted by their friends; as we have seen, too, lepers were always allowed to wander about and beg. The diagnosis in those days, moreover, was by no means certain, and there can be no doubt that lepers in the early stages of their disease were frequently overlooked.

In Norway there never has been any attempt at complete segregation. It is true that in 1856 there were nearly 3000 lepers altogether in that country, and that at the present time there are only about 800; but the number of the inmates in all the asylums put together has never at any time exceeded 800, and has been gradually diminishing during the last twenty-five years from that number to about 500. Until a few years ago, indeed, entrance into the asylums was not enforced, even in the case of indigent lepers; but in 1885 a law was passed to compel those to enter who could not be "isolated" at home; that is, who could not arrange in their own homes for a separate bed, separate clothes, separate utensils, etc. Indeed, the isolation and segregation of lepers in Norway is, even now, only partial; and in 1888 I found that the patients were frequently allowed to leave the hospitals and walk about the neighbouring roads. The individually "isolated" patients throughout the country must of course have even greater freedom.

It must be admitted, however, that it is only since these measures, incomplete though they be, have been adopted that leprosy in Norway has actually declined; nevertheless this decline may have been favoured by the improved sanitation, better food, and increased prosperity of the people.

In the Sandwich Islands, on the other hand, most determined endeavours have been made since 1865 to segregate the lepers completely; but the efforts have certainly not met with the success anticipated, either in the discovery of all the lepers or in the diminution of the disease throughout the country. Numbers of affected persons, to evade separation from their families, have been secreted; and in spite of the stringent laws leprosy went on steadily increasing in the islands until 1890 at any rate, since which date a slight decrease has been noted. The ultimate success of the Hawaiian segregation remains yet to be seen.

In most countries, indeed, where leprosy exists on a large scale, it may be taken for granted that a harsh measure of complete compulsory segregation is impracticable; but legislation, somewhat on the Norwegian lines, might very well be adopted in all places where the disease is endemic. In such countries lepers should be prevented from freely mixing with other people; from carrying on any occupation which may bring them into contact with the healthy, or any trade connected with food, clothing, and the like. Unless they can be maintained in their own homes with proper care and personal isolation, they should be treated in special hospitals, and mendicant lepers should be secluded in suitable institutions. In India and similar places leper farms or colonies might be established after the plans which work so well in Cyprus and at

Sialcote; and although matrimony need not be encouraged, there is no need to add further to the miseries of their existence by separating husband and wife, or even, in some cases, by prohibiting the marriage of lepers; for, as we have seen, the prospect of their procreating children is comparatively small. Any children born in such settlements should be brought up in separate orphanages.

PHINEAS S. ABRAHAM.

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P. S. A.

ACTINOMYCOSIS

AND MADURA FOOT

ACTINOMYCOSIS (ἀκτίς a ray, μύκης a fungus) is the name given on the authority of the botanist Harz (1) to a chronic infective disease which occurs in cattle. The parasitic nature of the disease was first[1] fully recognised, and its specific characters described by Bollinger (2).

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[1] Although the credit belongs to Bollinger of first securing general attention to the true nature of the parasite, and of showing it to be the cause of various diseases believed to be dis-

The name is derived from the characteristic appearance of the microparasite which is found in the affected tissues, and is the cause of the disease.

J. Israel (92) applied the name to a morbid condition which he first described as a specific disease in man, without recognising that it was identical with that which occurs in cattle.

Both in man and in cattle the disease presents symptoms of chronic inflammation, with the formation of granulation tumours which in many cases undergo suppuration.

History.—Until the year 1876 the true nature of actinomycosis had, with rare exceptions, been overlooked; cases in cattle were known under a variety of names, such as wens, scrofulous or tuberculous tumours, osteo-sarcoma, spina ventosa, and many others; and the positions in which the local affection was more commonly found were indicated by such names as wooden tongue, scirrhous, indurated, ulcerated tongue; polypus or lymphoma of the throat, etc.

It is probable, however, that actinomycosis is no new disease in man. As long ago as 1845, v. Langenbeck made drawings of some bodies found in pus from a case of caries of the vertebræ. The notes and drawings were published by Israel (92) more than thirty years later, and there can be no doubt that the case was one of actinomycosis.

In 1848 Lebert found and made drawings of some minute spherical bodies which were obtained from the thick gelatinous pus obtained from a case of thoracic abscess under the care of M. Louis. The drawings are excellent and unmistakable. The minute bodies, as large as a pin's head, yellow, with a tinge of green, are described as "corps particuliers trouvés dans du pus," without any definite indication of their nature or origin. As the result of a microscopical and chemical examination, M. Lebert arrived at the conclusion that, being neither albuminous nor fatty bodies, they might be the remains of some parasitic worm, and that the radiating, wedge-shaped bodies might possibly be hooklets, though he was unable to detect any traces of echinococcus or cysticerci.

In 1868 Rivolta (23) described some short, rod-like bodies, resembling those of the retina, which he had found in pus from a tumour of the lower jaw of an ox.

In 1871 Robin described and figured some yellowish grains which he had found in two or three cases of chronic abscess; he does not give any clinical history of the cases from which the pus was obtained, but describes the masses as being composed of minute elements swollen at one end, tapering at the other, and radiating from a common centre which consisted of granular matter.

In the following year Heller had under observation a case which he

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similar, many observers had previously recognised it in the tumours of cattle, some such as Hahn (3), Perroncito, and Rivolta, had suspected its vegetable origin, and Langenbeck had not only detected it, but described it as a fungus more than thirty years previously. See historical summary.

published later as one of "Actinomycosis, running the course of an acute infectious disease"; he made some drawings at the time, which doubtless were taken from colonies of actinomyces.

In 1875 Perroncito described the appearance of the micro-organism in a case of so-called osteo-sarcoma of the jaw, in an ox, and he suspected that it might be cryptogamic; and in this suspicion he was subsequently confirmed by Rivolta (24).

None of these observers, however, proved conclusively the true nature of the cases which they described.

In 1876 Bollinger (2) threw an entirely new light on the subject by the accurate description and identification of the characteristic micro-organism, which has given the name to the disease. His investigations applied only to cattle, but in the following year J. Israel described a similar affection in man, and in 1879 Ponfick (29, 30) brought forward strong evidence to prove the identity of the disease in man with that which occurs in cattle. Since this time the identity of the two diseases has been generally recognised, though no definite causal relation has yet been traced between them.

During the last ten years a large number of cases have been reported in almost every part of the known world, and the disease has been found to affect horses, dogs, pigs (31, 32), and elephants (33), as well as man and cattle. Illich (34) gives references to 421 cases in man, and Leith (36) gives tabular statements of nearly 450 collected from the same sources, so that the disease cannot now be regarded as of rare occurrence, whatever it may have been in the past.

The first case of actinomycosis suspected in this country was under the care of Mr. W. Knight Treves of Margate (39). The organism was not demonstrated, but the description given, and the fact that Mr. Treves recognised that the lesions were not scrofulous, nor due to any growth with which he was acquainted, make it very probable that his surmise was correct.

The first case in which the organism was demonstrated was admitted into St. Thomas's Hospital, 1st October 1884 (40). By employing Gram's method of staining I was enabled (41) to show the thread form of the micro-organism, the significance of which has been so fully recognised by subsequent observers.[1]

Since this date a large number of cases have been recorded in England; some of these are referred to more particularly below.

Pathological Anatomy.—The naked eye appearances of an organ or tissue affected with actinomycosis vary greatly according to the part diseased, the acute or chronic character of the process, and, probably, its greater or less contamination with pyogenic organisms. In some tissues the appearances differ but little from those of chronic inflammation; in others, such as in the liver or skin, they are often characteristic; in others again, notably in the lungs, the lesions have been frequently mistaken for tubercle.

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[1] Compare plates in the preceding paper (41) with those of Boström (43).

The illustration here given, taken from a specimen in the St. Thomas's Hospital Museum,[1] gives a very complete picture of a typical case of the disease in the *liver*. This organ, when affected, is the seat of a

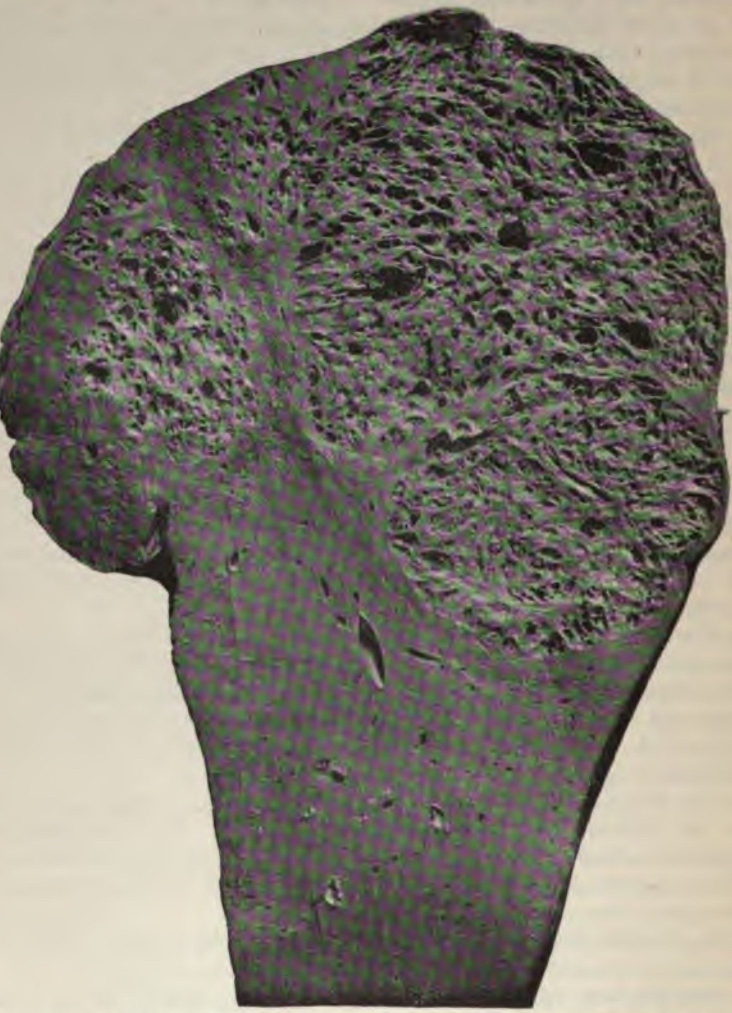

FIG. 1.—Section of liver affected with actinomycosis. From a photograph of specimen No. 1318 in the St. Thomas's Hospital Museum. In the plate the fibrous stroma is brought into greater prominence than was the case in the fresh state, partly owing to the specimen having been preserved in spirit, and partly owing to the fact that the contents have fallen out of many of the spaces into which the mass is divided.

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[1] For permission to take this photograph I am indebted to the kindness of Mr. S. G. Shattock. See also *St. Thomas's Hospital Reports*, 1885, p. 235, and compare Dr. Harley's drawing in *The Med.-Chir. Trans.* 1886, p. 156.

multitude of foci of suppuration, aggregated for the most part into large spheroidal masses, with outlying centres of inflammation. The larger masses are composed of an alveolar framework of fibrous tissue, the meshes of which are filled with inflammatory products, in the centre of which are embedded the characteristic minute yellow grains which are largely composed of the infective micro-organism.

The foci of inflammation vary much in size, from that of a pin's head to a minute point, but do not, as a rule, attain to any considerable dimensions. Their fundamental shape is spherical, but by pressure or contraction of surrounding parts they may be distorted to any form. Their walls, which are composed of fibrous tissue, in parts often deeply pigmented, are of varying thickness—the more chronic the inflammatory process, the thicker the walls. When the contents of this fibrous stroma are removed, a spongy mass, having a peculiarly worm-eaten appearance, is left.

In the *lungs* the lesions have a much less characteristic appearance. In some cases there is merely an acute primary bronchitis, with no sign of the reticular formation described in the liver (36). In others the tissue of the lung may be studded with gray nodules the size of a hemp seed, which exactly resemble tubercular nodules (49).[1] On the other hand, parts of the organ may be converted into tough, fibrous material, with an irregular interlobular distribution, enclosing here and there canary-coloured pultaceous masses. In a third class of cases there is diffuse broncho-pneumonia with some interstitial thickening, and a tendency to the formation of small abscesses and cavities. The general tendency of the disease in this as in other organs is, if *chronic*, to spread in one direction, leaving behind a track of cicatrising fibrous tissue; if *acute* (or more probably if largely complicated by the presence of pyogenic organisms), to form abscesses, with little tendency to cicatrisation (44).

The lesions in the *skin* are remarkable, and have been fully described by Dr. Pringle. The following description is taken from a case under his care. On the child's back there were livid, fleshy, sarcomatous looking outgrowths of mottled purplish red and yellow colour, varying in size from that of a split pea to a prominent bossy mass, rising abruptly to more than ⅞ inch above the level of the surrounding skin, and measuring 4 inches by 1 inch. To the touch the growths were soft, pulpy, fluctuating, and not tender. The skin over them was thinned, glistening, and semi-transparent. Every growth presented one or more crateriform, ulcerative openings, from which a clear, rather sticky fluid exuded in large quantities. In some of the larger tumours the ulcerative openings coalesced, forming superficial discharging sores, differing entirely from the hard-edged, punched-out, ragged ulcers which result from the breaking down of syphilitic or tuberculous masses.[2]

The naked eye appearances of lesions in other parts of the body need not be further particularised. Those in the *brain* are fully described by

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[1] For illustrations of Pulmonary Actinomycosis, see 37, 50, 52, 53.

[2] For illustrations of Actinomycosis involving the skin, see 35, 55, 56, 57, 58, 59.

Delepine (51, 60), and those found in the *digestive tract* by Leith (37*a*); while records of numerous cases will be found in the writings of Ponfick, Israel, and Boström; brief summaries of a large number of cases are also given by Illich.

The pus in most cases is characteristic; it varies in consistency but tends to be viscid, and to contain innumerable minute specks. These granules, which consist of the micro-organisms embedded in a layer of pus cells, are yellow or brownish by reflected, and often greenish by transmitted light. Under a lens they look like minute raspberries, being more or less spherical, and with a coarsely granular surface. In the majority of instances they are diagnostic of the disease.

If teased up in 0·75 per cent salt solution, and examined without staining, these granules are found to consist of four elements:—(*a*) inflammatory cells, (*b*) filaments, (*c*) bulbous or club-shaped, highly refracting bodies, (*d*) cocci. Either of the last two may be absent. In man filaments alone are sometimes present, in cattle the club-shaped bodies are the most frequently found, both in man and in cattle (in lesions which have been open to the air) pyogenic bacteria are as a rule present in varying numbers. The micro-organisms can be recognised under comparatively low magnifying powers (for example, Zeiss, Obj. D. Oc. 2, with a small stop), but it is preferable to use a $\frac{1}{12}$ oil immersion, and to stain the specimens.

Minute Structure.—On section a mature actinomycotic follicle under a moderately high magnifying power[1] is seen to consist (*a*) of a central core of irregularly distributed filaments, cocci in varying numbers, and in the older growths amorphous degeneration products. External to this core is (*b*) a ring of regularly arranged filaments radiating from a common centre. Surrounding this, again, there is (*c*) another ring more or less complete, consisting of club-shaped bodies through which bundles of radiating filaments from the inner zone are often seen to project. External to the clubs is (*d*) an envelope of inflammatory cells, amongst which there may be giant cells, in some instances containing portions of the fungus within. In certain positions, as in the liver, the inflammatory cells are again surrounded by a fibrous tissue framework, and this it is that gives to some actinomycotic lesions the remarkable honey-combed appearance described above.

The relative proportion of filaments, clubs, and cocci varies greatly in different cases and in different species. Thus in cattle a rosette of clubs is frequently present without threads, and in the young rapidly growing colonies in man, the threads may be found without clubs, but in man, as a rule, both threads and clubs are present when the growth of the fungus is active.

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[1] The affected tissues can best be examined after being hardened in absolute alcohol, and embedded in celloidin or in paraffin for section. The threads and cocci are best stained by Gram's method. The clubs are best stained with orseille or orange rubine. In lesions which have undergone calcareous or fatty degeneration, the structure of the organism frequently cannot be demonstrated without previous treatment with dilute hydrochloric acid and alcohol. For fuller details see bibliography (45, 51*a*, 15). For the microscopic appearances of actinomyces reference may be made to the following plates, see bibliography (42, 46, 61, 100, 54, 96).

Anatomical Distribution.—In 393 cases collected by Leith (*loc. cit.* p. 174 *et seq.*) the primary seat of the disease is recorded as follows:—Head and neck, 207; tongue, 13; pulmonary, 52; abdominal, 88; skin, 10. In the 23 remaining cases the point of infection was doubtful.

The numbers given by Illich agree closely with those above. He found that in 421 cases the head and neck were primarily affected in 218, the tongue in 16, the lungs in 58, the abdomen in 82, the skin in 11, the point of infection was doubtful in 29.

Of these cases, in which the primary seat of the disease is known, it will be seen that more than half occurred in the head and neck.

Rare instances have been recorded in which the primary seat of the disease is believed to have been in other parts, such as the brain (4), the reproductive system (63),[1] and the orbit,[2] but it is obvious that in some of these cases the organism must have found entrance into the body at some distant point, and that the seat of maximum disease, rather than the point of inoculation, was discovered.

Of 405 cases recorded by Leith, of which the sex is known, 295 are males and 110 are females, so that it would appear that the disease is far more common in men than in women.

Invasion.—The means by which the fungus gains entrance into the tissues has been the subject of much inquiry and many ingenious hypotheses. In some cases it would appear certain that it is conveyed by grain (corn or barley) or some foreign body, which has caused a lesion of the mucous membrane of the digestive (47, 69) or respiratory (70) tract, or skin (71); but no evidence has as yet been brought forward to show that an organism, found outside the body, has been cultivated and successfully inoculated into an animal with the reproduction of actinomycosis. What are supposed to have been clumps of actinomyces have been detected in the crypts of the tonsils (66) and in the hollows of decayed teeth (72), and have been considered a possible source of infection. In one instance Israel (73) found a piece of what he believed to be dentine from a tooth embedded in an actinomycotic focus in the lung. Soltmann records a case in a boy who accidentally swallowed an ear of barley grass, and who subsequently suffered much substernal pain. An abscess formed in the sixth right intercostal space, between the spine and scapula, and the ear of grass was found in the pus, which was evacuated; the pain, however, continued, and after a time the case proved to be one of actinomycosis. Boström (43) demonstrated some remains of a cereal in the lesions found in eleven cases which he examined; other cases are recorded in which the disease has followed a wound with a splinter (76), or has occurred in those pursuing agricultural occupations; and Jensen (78, 82) has recorded an epizootic which occurred in Denmark amongst a herd of cattle fed on barley grown on land reclaimed from the sea. With regard to invasion by the digestive tract it may be noted that Leith (38) records cases of actinomycosis of the mamma in a cow, and Müller (77) records two similar cases in women, so that the possibility of infection through milk cannot be disregarded.

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[1] See *System of Gynæcology*, p. 798.

[2] Communicated by Dr. W. B. Ransom, of Nottingham. See also two cases of ocular actinomycosis, *Centralblatt für Pathologie*, Jan. 15, 1895.

The direct transmission of the disease from one individual to another is rendered probable by a case recorded by Baracz (79), in which a woman suffered from actinomycosis of the face after being brought into close relations with a man who was similarly affected; but such cases are rare, and no case of direct transmission from animal to animal, nor from animal to man, nor *vice versâ*, has been recorded. In a report from the Chief of the Bureau of Animal Industry to the Secretary of Agriculture in the United States, it is stated (81) that twenty-one healthy cattle were kept in close quarters with others suffering from actinomycosis without in any case showing signs of infection. From this it is argued that the disease can be accidentally transmitted direct from one individual to another only with considerable difficulty, and on rare occasions, and this has been borne out by the observations of other investigators of large experience such as Dr. M'Fadyean (82).

Experimental transmission of the disease from one animal to another, and from man to animals both directly and after artificial cultivation, has been successfully accomplished (96).

The first successful experiments by direct inoculation seem to have been carried out by Johne (67) in 1880. Three years later J. Israel (74) succeeded in transmitting the disease from man to a rabbit by direct inoculation. He implanted a piece of granulation tissue from a patient suffering from a thoracic abscess, due to actinomycosis, directly into the peritoneal cavity of a rabbit. About three months afterwards the peritoneal cavity was found studded with tumours of various sizes. The tumours contained the fungus surrounded by granulation tissue, and the other elements usually found in the lesions characteristic of the disease.

These experiments have been repeated and confirmed by (2) Crookshank (100, 62), Rotter (84), and others, and the transmissibility of the disease from cattle to cattle by direct inoculation has been demonstrated by the researches of Johne (68, 66) and Ponfick (95). These latter investigations tend also to show that cattle are more susceptible to inoculation than either dogs or rabbits.

The earliest successful inoculation experiments with the fungus artificially propagated outside the body were carried out by Wolff and Israel (96). Eighteen rabbits and three guinea-pigs were inoculated by the introduction of a small portion of the culture into the abdominal cavity. Of twenty-two animals used for the research two only did not contract the disease, one a rabbit which had been inoculated with sterile agar as a control experiment, the other a sheep in which the inoculation failed to produce any result. In all the cases in which the experiment was successful the peritoneal tumours were similar to those found in the direct inoculations of Johne and Ponfick mentioned above. The small masses were surrounded by a capsule, and had a pulpy interior; in the larger the capsule was dense, and the interior of the mass was divided by fibrous septa, the interstices of which contained the minute grain-like masses so characteristic of actinomycotic lesions. In many of the specimens examined both the club and thread forms of the fungus were detected, but in some of them the threads were predominant, as is frequently the case in man. That the fungus was alive, and had really been instrumental in producing the disease, was further proved by the fact that actinomyces taken from the tumours was, in four cases out of six, successfully cultivated through many generations on agar; and further, that in one of the animals experimented upon, two metastatic actinomycomas developed in the substance of the liver, the contents of which very closely resembled similar lesions in man (85).

The method by which the disease spreads within the body is in most cases by a gradual invasion of the tissues surrounding the point of inoculation. At the seat of infection minute points of inflammation are found, which extend at their periphery, and unite to form large areas of granulation tissue. These masses tend to break down in one direction and heal in another, leaving behind dense cicatricial bands. The process often differs widely from that of simple inflammation. In its progress the disease disregards anatomical boundaries, and invades one tissue after the other, the direction of spread being determined, not by similarity of tissue, but by contiguity, so that all tissues and organs may be alike involved. Thus a focus of disease in the liver may spread to the diaphragm, and, perforating it, lead to the formation of an empyema, or to the invasion of the base of the lungs. The soft parts become matted together, and as the disease extends long sinuses are formed which, by the discharge of the characteristic pus, often give the first intimation as to the true nature of the disease.

The lymphatics show no constant tendency to become involved in the disease, and when the glands are enlarged the swelling is, as a rule, due to simple inflammation rather than to invasion by the micro-organism.

Metastases occur in a small proportion of the cases, and in this way large areas may be simultaneously infected, as in a case recorded by Ponfick, in which the left jugular vein was perforated by a mass of the organism, with the subsequent formation of actinomycotic infarcts in the lungs, spleen, brain, and heart (30).

Cultivation.—The organism has been successfully cultivated outside the body by many observers. Boström,[1] in his classical paper, gives the results of several hundred cultures which he made from human and bovine actinomyces. He was successful both under aerobic and anaerobic conditions at 37° C., using gelatine bouillon and agar. He did not, however, succeed in reproducing the disease in animals.

In this country Dr. Crookshank has carried out a large series of cultures which show that the organism grows readily under suitable conditions, the separate growths spreading peripherally, and forming by their amalgamation larger areas with crescentic or circular outlines like intersecting fairy rings. After a few weeks the growth becomes covered with a whitish or yellowish powdery efflorescence, which under the microscope is found to be composed almost entirely of spore-like bodies. When cultivated on agar the young colonies of actinomyces show under the microscope a tangle of branching threads, some straight, some twisted, and some with bulbous extremities. As a rule no true clubs, such as are found in animal tissues, develop in cultures, although expansions of the threads having a somewhat similar appearance have been found by Boström in cultures grown under anaerobic conditions. He attributed this to the exhaustion of the nutritive material in the culture medium, and considers it as evidence that the clubs are involution forms.

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[1] For coloured drawings of cultures of actinomyces, see References Nos. 86, 48.

Biological Position.—Actinomyces was originally believed to be a mould, of which the clubs were the asci or gonidia, and the threads mycelium; but recent researches of Boström, Wolff, and Israel have led them to the conclusion that the clubs are involution forms, and that the method of reproduction is by the formation of spores in the filaments, or by their transverse fission. Dr. Crookshank (to whom I am indebted for much help and information) is, on the contrary, of opinion that the clubs are not degeneration forms, but mucilaginous expansions of the sheath of the threads, which become highly developed when the organism is growing in animal tissues; and (though he has not traced the metamorphosis through all its stages) he believes that the spore-like bodies which are seen in affected tissues, and form freely on the surface of mature cultures, are really spores, and that the threads develop directly from them.

Comparative Biology.—The biological position of actinomyces is one of much interest, and has been the subject of wide differences of opinion, owing to the fact that in some points it resembles a bacterium (Schizomycetes), in others it resembles a mould (Hyphomycetes). The main points of the discussion are summarised by MM. Sauvageau and Radais, who conclude that the organism is not a bacterium, but is in reality a streptothrix (Cohn), and belongs to the higher fungi—it has no sheath, is branched like a mycelium, the filament dividing into rods and granules, while spores are formed by the segmentation of filaments which are slightly larger than those which are growing freely. On such grounds actinomyces is classed by Sauvageau and Radais amongst the Hyphomycetes, sub-order Mucedinæ, to which group it has been proposed, as is indicated below, to give the generic name of Oospora (Wallroth). Dr. Crookshank maintains that this group of organisms is intermediate between the bacteria and the higher microfungi.

Comparative Biology and Pathology.—Since actinomycosis was first brought into prominence as a definite disease, numerous records have been published of affections which, though probably not identical, are closely allied to it and to one another, both in their course, clinical symptoms, and in the nature of the organism found in the diseased tissues. Of these the most important is mycetoma, or Madura foot, which was described as a "fungus disease" by Dr. H. Vandyke Carter, some thirty years ago.

Mycetoma presents many points of resemblance to actinomycosis (7, 10). It is a chronic, locally spreading inflammation of the foot, or more rarely of the hand, resulting in the destruction of the parts involved and in a great overgrowth of connective tissue. There are two varieties of the disease, the one characterised by the presence of brownish or yellowish white particles like fish roe (the pale or ochroid form), the other by black or dark brown masses, varying in size from that of an hemp seed to that of a walnut (9)—the melanoid form. Both of these contain a fungus[1] which there are grounds for believing to be the cause of the disease. Clinically there are marked differences between mycetoma and actinomycosis. Mycetoma almost invariably attacks the hand or foot, rarely a limb, and Carter (6), with his wide experience of the disease, doubts whether the viscera are ever the seat of secondary deposits. In actinomycosis, on the contrary, the extremities are hardly ever attacked, and the viscera are frequently the seat of the disease. Again, mycetoma is essentially a disease of hot climates, very few cases having been recorded in Europe (12, 13). Actinomycosis is a disease of temperate latitudes. An organism has been cultivated from the pale variety of mycetoma which differs in many particulars from actinomyces (14). The fungus from the black variety has not been cultivated, but there are grounds for believing that it is similar to that which is found in the yellow masses, only in a state of pigmentary degeneration. From such investigations as have been made up to the present time, it would seem probable that the organisms found in actinomycosis and mycetoma are closely related, but the superficial resemblances of structure and of their reaction towards diseased tissues are not sufficient to establish their identity.

Nocard (16), Eppinger, Hesse, and Schmorl have also described pathological conditions occurring in man and animals which seem to be caused by organisms closely allied to, but not identical with actinomycosis. MM. Sauvageau and Radais have proposed a generic name for this group, based on what they believe to be the biological position of the micro-organisms. They suggest for Actinomyces bovis (et hominis) the name Oospora bovis (et hominis); for Nocard's fungus, Oospora farcinica; for Eppinger's, Oospora asteroides, etc.; and Dr. Kanthack (7*a*) suggests the name of Oospora Indica for the parasite of Madura foot.[2] This classification and nomenclature has not hitherto received general acceptance.[3]

The **clinical course** of actinomycosis is generally chronic, but in exceptional cases there is rapid dissemination, owing to the fungus having found entrance into the vascular system. Sometimes it pursues the course of an acute infectious disease (8, 26), or even pyæmia, but such acute cases are rare, and any considerable pyrexia, suppuration, or septic infection is as a rule caused by accidentally associated pyogenic organisms. But the manifestations of the disease may be as protean as the organs which the disease attacks are various. When one viscus alone is affected there is often no guide to the real nature of the disease. It is for this reason that so many of the cases recorded have only been recognised after death; during life they have been regarded as abscesses, empyema, appendicitis, vertebral caries, tuberculosis, sarcoma, etc. In a large proportion of cases no certain diagnosis can be made without the detection of the fungus in the discharges. When the skin is involved, the appearances of the raised, pulpy, fleshy masses, with minute fistulous openings discharging a thick gelatinous pus, are often characteristic. If the pus be shaken up in a test-tube with a little salt and water, the actinomycotic grains will be seen, often in hundreds, like minute yellowish or greenish specks clinging to the sides of the tube. The presence of these grains renders the diagnosis certain so far as the general nature of the affection is concerned; but, from what has been said above, it follows that the more precise differentiation of the species of fungus must be decided by microscopical examination. The pus is generally without odour, and tends to be greenish or yellowish; but in actinomycosis of the lungs the sputum is often offensive, and the case resembles one of bronchiectasis.

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[1] Compare Lewis and Cunningham (11). The view is taken that the fungus is not causally related to the disease.

[2] A concise account of the differences between the organisms of Actinomyces and Madura foot will be found in M. Vincent's paper, *loc. cit.* p. 150.

[3] Two other organisms belonging to the same group (Oospora Metchnekowi and Oospora Guignardi) have been described; the one was detected in water, the other in the air.—Sauvageau and Radais, *loc. cit.* pp. 252-257.

Prognosis and Treatment.—When uncomplicated and local the disease is little dangerous, except from the mechanical interference which the neoplasms may exert on organs essential to life. Suppuration, and metastasis, with their consequences, are the dangers which should excite most apprehension.

Just as in tubercle, the affected tissues may become cicatrised or calcified, and the disease may in this manner be cured, yet in a large proportion of cases it is steadily progressive, and ends fatally from exhaustion.

Until recently it was believed that no drug could exert any curative influence on the lesions of actinomycosis, and that the only remedy was complete excision of the affected part. Such surgical treatment has in a few cases been successfully carried out. Other means, such as injections of tuberculin (87) and "bacterien protein" (88), injections of iodine, and decomposition with an electrical current (57*a*), have been tried and found to be of temporary benefit. Many years ago Thomassen first used iodide of potassium, and the local application of iodine to the disease in cattle. In 1891-92 a series of cases were similarly treated at Chicago (81), of which 63 are said to have recovered, and Nocard (17), M'Fadyean (83), Buzzi, and Ransome have recorded cases in man in which the same drug was used with marked success. Such being the case, the treatment with iodide of potassium in increasing doses should have a fair trial. The dose in man should reach 45-60 grains, in cattle 240 grains per diem.

The organism, fortunately, has a low vitality, and is readily affected by iodoform, corrosive sublimate, and other antiseptics; moreover, the spread of the disease is usually slow, so that in any case in which the lesion is within reach of local treatment, and there is no deep-seated suppuration, a favourable prognosis may be given.

Theodore Dyke Acland.

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T. D. A.

DISEASES OF UNCERTAIN BACTERIOLOGY

(*a*) NOT ENDEMIC

18. MEASLES
19. RUBELLA
20. SCARLET FEVER
21. VARICELLA
22. VARIOLA
23. MUMPS
24. WHOOPING-COUGH
25. SYPHILIS

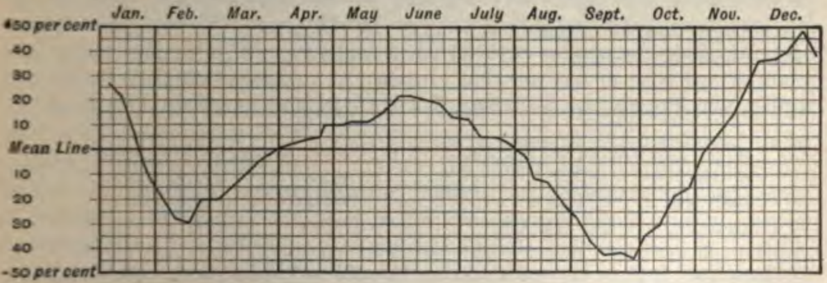
MEASLES

SYNONYMS.—*Morbilli;* Fr. *Rougeole;* Ger. *Masern.*

MEASLES is a specific, infectious, eruptive fever, characterised by coryza and catarrh of the upper part of the respiratory tract, and by a peculiar blotchy eruption on the skin.

Statistics.—The liability of all races of mankind to measles appears to be equally great. The sexes suffer equally. No age, however advanced, affords protection, and infants have been born with the rash. It is true that a far larger number of cases occurs among children than among adults, but this is due to the fact that in civilised countries few individuals escape infection during childhood.

In Great Britain about 60 per cent of the deaths from measles occur in children under two years of age; about 90 per cent among those under five, and about 98 per cent among those under ten. The mortality under six months of age is comparatively small, and it is probable that about half the individuals who die of this disease are children between the ages of six months and two years. Persons appear to be attacked with equal frequency at all ages in isolated communities—such as those of Fiji and of the Faroe Islands—into which the infection of measles is introduced for the first time or after a long interval.



The mean line represents an average weekly number of 34 deaths.

Fifty years 1841-90.

From the *Annual Summary* (London and other great towns) 1890, issued by the Registrar-General.

The statistics of the Registrar-General show that measles in England and Wales attains a maximum at two periods in each year—in June and December; but there are also years of epidemic prevalence, when the mortality reaches an exceptionally high level. Dr. Whitelegge states that in English towns the interval between these epidemic outbursts is usually about two years, but that it is occasionally six months more or six months less—owing, as he suggests, to the fact that the seasonal curve shows two maxima. He believes, also, that there is distinct evidence of an epidemic wave of longer period, recurring at intervals of about ten years, when a very high mortality is produced. He points out also that in populous places the fatality of measles may become gradually greater through a series of epidemics, until a rate double or treble that of the ordinary seasonal maximum is reached.

The case mortality of measles varies much in different epidemics, and in relation to the age, previous state of health, and sanitary surroundings of the patient. The mortality from this cause among children in foundling institutions may reach an enormous proportion: thus in the Hospice des Enfants Assistés in Paris the deaths reached an annual average of 44 per cent in the four years 1882 to 1885 (8).

While it is true that there is evidence that the severity of the disease itself varies in different epidemics, a much more important factor appears to be the goodness or badness of the hygienic conditions under which the children are placed. Chief among the causes of a high mortality are overcrowding and insufficient ventilation. The mortality in the Paris institution already mentioned has been reduced at least one-half by systematic isolation not only of the children suffering from measles, but also of children suffering from measles complicated by broncho-pneumonia from other children with measles, but not presenting this complication. In an epidemic of a mild type the mortality among children treated at home may be almost nil; though the deterioration of health due to the disease, and in particular the special liability to the development of fatal tuberculosis which it produces, exercise some influence in increasing the death-rate of a district. The mortality of persons attacked with measles varies greatly with age. It is highest between the ages of six months and two years, and falls rapidly after the fourth year. Henoch had among hospital cases a mortality of 55·5 per cent among 133 children under two years of age, and of 9·5 per cent among 161 children over two years old. Gannelon's statistics from the Hospice des Enfants Assistés are as follows:—

0–6 months,	23·68 per cent	3–4 years,	13·66 per cent
6–12 ,,	57·77 ,,	4–5 ,,	6·20 ,,
1–2 years	53·94 ,,	5–10 ,,	2·4 ,,
2–3 ,,	27·73 ,,	10–21 ,,	0·0 ,,

Embden, during an epidemic at Heidelberg, had among cases treated at home a mortality of 14 per cent in children one year old or under; 7·5 per cent in children from one year old to four, and 2·2 per cent from four years old to thirteen. The main cause of the high mortality in hospitals among children under four years old is broncho-pneumonia; though the occurrence of membranous pharyngitis or laryngitis is also responsible for a large number of deaths.

Pathology.—The mode in which the infection of measles is contracted is in most cases personal intercourse. The infection is perhaps greatest during the earliest stage. It is present at the onset of the prodromal symptoms, possibly even a little earlier, and persists down to the time when the rash fades. Thereafter it declines rapidly. Though infection may be derived—especially, perhaps, if desquamation is well marked—from a person who has recovered sufficiently to resume his ordinary occupation, it is rarely that infection can be traced to a convalescent later than three weeks after the commencement of his attack; though infection may persist longer in complicated cases. On the other hand, it is probably as great on the first day of the prodromal symptoms, even though these be slight, as at any subsequent date. It is seldom retained long by fomites or utensils. Though it is highly probable that measles is due to a specific micro-organism its nature is as yet unknown. Canon and Pielicke, in 1892, described a small bacillus in the blood, and obtained cultivations; their results have not obtained general acceptance, and it is possible that the bacillus isolated by them was in reality that of influenza. Czajkowski, however, states that he has found a bacillus, which he believes to be the same, in the blood of fifty-six cases of measles—a long slender bacillus with blunt ends—and has cultivated it from nineteen. In mice it produces septicæmia, and the evidence of its place in the causation of measles is very slight as yet. Dohle (6) has described flagellated protoplasmic bodies in the blood, sometimes in the blood corpuscles, but his observations are unconfirmed. The important part which infective organisms play in the complications which are in the main responsible for the mortality of measles will be considered subsequently.

The eruption is produced by congestion and infiltration of leucocytes. The infiltration is greatest about the vessels, the sebaceous glands, and the sweat glands. When the congestion is sufficiently intense, small hæmorrhages may occur into the derma or subcutaneous tissues. There is also some infiltration into the superficial papillary layer. Localised colloid degeneration of the cells may ensue, producing the false appearance of a vesicle crowning a papule produced by the intense congestion about the centre of degeneration.

It is difficult to distinguish the visceral lesions due directly to the infection of measles from those produced by secondary infections. The catarrh of the mucous membrane of the eyes, nose, mouth, pharynx, larynx and bronchi, favours the development of secondary processes due to infection—in the mouth, nose, and larynx by pyogenetic organisms, in the lungs by the various organisms associated with pneumonia, and in the larynx by "diphtheria." The broncho-pneumonia does not differ from that not secondary to measles, except perhaps by the greater rapidity with which it develops, and a greater tendency to the formation of pus. Cornil and Babes (5) have described a special form of pneumonia the primary lesion of which appears to be an inflammation of the lymphatics and interalveolar connective tissue; fibrinous exudation occurs at first in these situations, and involves the alveoli later. On account of this peculiar distribution it is held that this form of pneumonia is due to the primary infection of measles. The exudation it produces undergoes granular and then fatty degeneration, leading to the formation of caseous areas which simulate tuberculosis. Tuberculous disease of the lungs is found in a large proportion of children, over five years of age, who die some little time—weeks or months—after the onset of measles. In some of these cases there is true miliary tuberculosis, which may involve not only the lungs but also the spleen, meninges and other organs; in others there is tuberculous caseation of the bronchial glands, or caseous areas in the lung, though these are often masked by attendant broncho-pneumonia. Inflammatory engorgement of the bronchial lymphatic glands is the rule, and some simple chronic enlargement may persist, though tuberculous adenitis is probably the more common sequel.

Incubation.—The interval between exposure to infection and the onset of the prodromal symptoms is usually ten days, but may be as short as five or perhaps four days. On the other hand, it may be as long as fourteen days, in which case the rash would not appear until the seventeenth, eighteenth, or even the nineteenth day after infection. Though the period of about fourteen days from exposure to the appearance of the rash is that met with in the vast majority of cases, it is important to recognise that it may be four or five days longer, since such exceptional cases must be taken into account in estimating the period for which a susceptible person who has been exposed to infection should be isolated from other persons who have not had the disease. An interval of a full fortnight must be allowed; and at the end of that time the person must be free from fever, catarrh, and photophobia before it can be said that he has escaped infection.

Symptoms.—*Prodromal Stage.*—From eight to ten days after exposure to infection the patient begins to suffer from catarrh of the mucous membranes of the eyes, nose, pharynx and larynx. The temperature is raised (102° to 104° F.), cough is troublesome, but, beyond a little scattered sibilus, examination of the chest reveals no physical signs. The face is puffy and pale, or a little dusky. The eyes water, the sclerotic is injected, and the palpebral conjunctiva red and swollen; there is some photophobia, it may be much. A thin, watery fluid, discharged from the nose, irritates the upper lip; the voice and cough are hoarse; the tongue is covered by a white fur, its edges are red, and the papillæ enlarged. The mucous membrane of the mouth and pharynx is red and œdematous. The aspect of the child at this stage, if not entirely characteristic, is at least extremely suggestive. On the second day the temperature is higher, the secretion from the nose and naso-pharynx is muco-purulent, and the glands, especially those behind and beneath the lower jaw, are enlarged and tender. An eruption of closely-set red points may be visible on the palate and the buccal mucous membrane. The child as a rule is extremely irritable, owing in great part to the distress caused by the photophobia and by thirst. Shivering fits, or, in young children, convulsions, may occur during the prodromal stage; these, however, are generally slight and of short duration. In some epidemics the patient during the prodromal stage remains in a dull, somnolent state. During this period there may be marked symptoms of laryngitis, or in some cases, especially in quite young children, attacks of laryngismus. In some epidemics epistaxis has been observed in a large proportion of cases, occasionally to a serious extent.

Eruptive Stage.—The eruption appears on or about the fourth day, often in the night between the third and fourth days. It is noticed first on the forehead, at the edge of the hairy scalp or behind the ears; and a little later on the cheeks, chin, and neck: after some hours it spreads downwards, reaching in succession the trunk, arms, and lower limbs. It begins to decline in about twenty-four hours, so that it may be fading on the face while yet it has not reached its full intensity on the lower limbs. Occasionally there are distinct short intervals between the appearance of the rash on the face, the trunk, and the limbs. In other cases, after coming out well on the face, it fades rapidly and does not reach the trunk. This rapid disappearance of the rash is sometimes observed in very mild cases; sometimes it marks the onset of serious visceral complications, as the general condition of the patient, the temperature, and the physical signs may indicate. The rash, especially that on the face, is at first a diffuse redness, or consists of closely-set red points; but in a few hours small, round, red spots, which give to the finger the sensation of very low flat papules, form in the affected parts. As they enlarge they form patches, often crescentic in form, with a scalloped edge, and assume a dusky red or mulberry colour. When they reach this stage the colour of the patches is not discharged by pressure, and small ecchymoses frequently appear. While the rash is coming out the catarrhal symptoms persist, or are somewhat aggravated; and the laryngeal symptoms in particular may become more marked, owing to extensive catarrh of the mucous membrane, which may cause even a slight reddening of the vocal cords themselves.

The eruption may be irregular in character, intensity, and distribution. An unusual amount of congestion may, by throwing up the hair bulbs, give rise to a papular appearance, which, if the rash be scanty, may resemble the early stage of varioloid. The rash at its first appearance may be so intense and confluent as to cause an almost uniform reddening of the face, neck, and chest, so as to suggest scarlet fever; but, even if the reddened areas cannot be made out to have a well-defined scalloped edge, the nature of the eruption will be evident after a few hours. In rickety children and in warm weather the true rash is often preceded by sudamina. In children infested by fleas or lice the general tint of the rash may be deepened by very numerous petechiæ or by "marbling." Ecchymoses, especially on the back and thighs, are frequently produced in cachectic children; in whom also the rash is commonly discrete and pale.

Physical signs of bronchitis are seldom absent during this stage. Sibilant rhonchi may be heard in all parts of the chest, especially in the interscapular region, and give way after a short time to moist râles.

The expectoration, seldom observed in very young children, is at first clear and stringy; later it becomes purulent and nummular. In both stages it is remarkably viscous and tenacious. The child continues to be extremely thirsty, but refuses food. Diarrhœa of foul-smelling slimy stools very commonly occurs during the eruptive stage, either at the onset of the rash or as it fades. The child is restless and peevish by night, but often sleeps much in the day.

As a rule the eruptive stage lasts three or four days, but may continue for six.

Convalescent Stage.—After an uncomplicated attack convalescence is as a rule rapid. As the rash fades thirst diminishes, the nasal discharge decreases, sleep becomes natural, and appetite returns. Cough and some photophobia remain for a few days more; but the signs of bronchitis clear up rapidly, and at the end of ten days or a fortnight from the onset of the prodromal symptoms the child may appear to be quite well. A little fine branny desquamation may generally be observed, especially about the face, neck, and waist; occasionally it is very extensive and detached in flakes, especially if there has been some miliary eruption.

Departures from the usual Type.—*Mild Forms.*—The symptoms of the prodromal period may be so slight as to pass quite unobserved. Occasionally the period is prolonged to six or eight days. The disease sometimes appears to abort early in the eruptive stage, and convalescence begins about the second day of that period. Occasionally, during an epidemic of measles, cases characterised by fever, coryza, bronchitis, and gastric derangements, but without any rash, are met with; as these patients are found to be immune on subsequent exposure to the infection of measles a possibility of the occurrence of measles without rash must be admitted.

Malignant Forms.—Though measles, if uncomplicated, is, as a rule, benign, it may be a most severe disease; owing either to the intensity of the infection or to the cachectic or unprotected condition of the individual attacked. Several forms of malignant measles are met with, and are to be distinguished from those cases which become severe owing to complication.

In cases of the *Typhoid* type there is said to be retrocession of the eruption; that is to say, the rash either does not come out well, or its evolution is suddenly stopped. Simultaneously the pulse rises to 130 or 140, the respirations to 60 or 80, the temperature to 104° or 105° F.; the tongue becomes dry, the lips cracked, the skin burning, and the amount of urine is much diminished. The profound nervous disturbance present, which must be attributed to toxæmia, is evidenced either by extreme depression and somnolence, or by excitement—severe convulsions in children, and delirium in the adult. The state of excitement may pass off as rapidly as it developed, or the patient may sink into a comatose state, which rapidly ends fatally. Between these two extremes every degree of severity may be observed. In some epidemics, especially in schools and barracks, cases occur in which the patient, at or about the time of the outbreak of the rash, becomes cyanosed and suffers from severe dyspnœa. Cough is frequent, and the expectoration, if present, is frothy. There are at first no physical signs to account for this condition; but after a few hours fine mucous râles are heard everywhere in the chest, and the patient succumbs to what is commonly called capillary bronchitis. These cases are probably examples of the severest form of the special type of pneumonia described by Cornil and Babes. In the adult death may be very sudden, and due to syncope. The eruption is scanty, or fades at the onset of the dyspnœa. To this form the term *suffocative* has been applied. In some cases, presenting symptoms of the typhoid form, the rash assumes a livid colour; and hæmorrhages, more or less extensive, take place into the skin. Epistaxis and hæmorrhage from the mouth and bowels may occur. To this form, which occurs in cachectic subjects, the term *hæmorrhagic measles* properly belongs. The extremely severe examples of this form described by the older writers as "black measles" are now seldom or never met with: and as Fagge observes, "One is almost inclined to suspect them of having mistaken cases of hæmorrhagic small-pox for this disease."

The term *secondary measles* is applied to attacks occurring in persons whose health has been enfeebled by a recent attack of typhoid fever or diphtheria, or by tuberculosis, or other general malady producing cachexia. In such persons the disease may run a mild course, but on the other hand it may be of exceptional severity. The prodromal symptoms are not well marked; the eruption is scanty and dusky, or purpuric; the temperature is high and continuous; vomiting and diarrhœa are common, and in young children broncho-pneumonia develops.

Relapse.—It has sometimes been asserted that relapse is of common occurrence in measles, but it seems clear that a true relapse is a very rare event. Some of the cases quoted as examples of relapse are really instances of irregular development of the rash; others rest, apparently, upon an error of diagnosis—the first or the second eruption being in reality that of "German measles."

Temperature.—The ordinary temperature curve of measles shows a double summit. The temperature rises rapidly at the onset of the prodromal symptoms, reaching a first maximum of 102° to 104° F. within the first twenty-four hours; for the rest of the prodromal stage it is at a lower level, with evening exacerbations and morning remissions, which may even reach the normal. The lowest point is touched on the morning of the second or third day. The temperature then mounts until the appearance of the rash, when it attains its second maximum, which is generally higher than the first, and may be as high as 105° to 106° F. It does not remain long at the maximum, and usually falls rapidly on the third day of the rash, reaching the normal standard probably on the morning of the fourth day. The fall to normal may be delayed for one or two days: it may be so rapid as to constitute a true crisis, which may be accompanied by profuse sweating, and even by collapse. In other cases the fall is much more gradual, and may extend over three or four days of gradual descent. The curve is much modified if the patient be already suffering from some chronic febrile disorder, or by the onset of complications. In the former case it is still frequently possible to detect the double maximum; in the latter the fall, after the eruption has come out, is replaced by an elevated temperature, due to broncho-pneumonia or to the particular complication under which the patient labours. Sometimes the rapid rise at the onset of the prodromal symptoms cannot be detected, and the curve mounts, with morning remissions, to a single maximum on the first day of the eruption.

Pulse.—The pulse increases in rapidity from the onset of symptoms until the eruption appears, when, in uncomplicated cases, it begins to fall. In uncomplicated cases it seldom exceeds 120 in children, and 90 in adults.

Complications.—*Laryngitis.*—Some degree of catarrhal laryngitis ought, perhaps, to be considered rather as a symptom than a complication of measles. It usually decreases soon after the rash appears. In other cases the symptoms increase in severity; voice and cough become first hoarse and then toneless, and movements of or pressure on the larynx excite pain. The expectoration becomes blood-stained. Necrosis of the cartilages may ensue, or œdema glottidis. Such an event is rare; but membranous laryngitis, especially in schools and asylums, is a not infrequent and very fatal complication. It may come on either during the eruptive stage or as late as the second week. In some cases it is due to true diphtheria; in others, perhaps the majority, to infection with pyogenetic cocci. The symptoms—which need not be described here—are practically identical; but it may be observed that the membrane produced by pyogenetic cocci is as a rule more diffluent or friable than that produced by true diphtheria. The false membrane may invade the fauces and tonsils. The onset of symptoms is commonly more insidious than in primary diphtheria; attacks of dyspnœa are less frequent, and there is less warning of the approach of asphyxia. The results of tracheotomy are extremely bad, and even when some temporary improvement takes place the wound itself is very apt to become the starting-point of phlegmonous inflammation.

Bronchial catarrh, be it more or less, must be considered one of the ordinary symptoms of measles; but the smaller bronchi and the pulmonary tissue are liable to become involved at any stage of the disease. Reference has already been made to those acute cases, called suffocative, in which the lungs become involved in the prodromal stage; but, short of these, cases occur to which the term "congestion of the lungs" is commonly applied. The respiration is hurried, there is slight cyanosis, the pulse is rapid and soft, and everywhere over the chest small moist crepitations are heard; the breath-sounds, however, are not bronchial, there is no true fine crepitation, and resonance is not deficient. The cases resemble "capillary bronchitis," but differ from it, inasmuch as all the symptoms and physical signs diminish rapidly at the time the rash appears or soon afterwards. In a few cases only does pneumonia appear. In a small number the symptoms described persist throughout the stage of eruption, and until the period when convalescence ought to begin. Such an occurrence is very suggestive of the lighting up of tuberculosis.

Broncho-pneumonia, the most fatal complication of measles, first becomes evident as a rule during the eruptive stage. It may begin about the time when the eruption comes out, or even earlier; or its onset may be deferred until it is hoped that convalescence is about to commence. The symptoms do not differ from those of primary broncho-pneumonia; but it should be borne in mind that in a child suffering from measles the lesion is more apt to be progressive. This broncho-pneumonia is to be attributed to a secondary infection. The catarrh determined by the primary infection of measles appears to favour the growth of certain pathogenetic organisms, chief among which are the pneumococcus, the streptococcus pyogenes, and the staphylococcus pyogenes aureus. All of these microbes may be found in the secretions of the mouth, nose, and larger bronchi, even in health; but they are more frequently present in children suffering from measles. The so-called subacute or chronic pneumonia of measles, which comes on as the eruption subsides, or later when convalescence appears to have begun, is almost invariably a tuberculous process; there is irregular pyrexia with evening exacerbations, persistent cough, and signs of localised pneumonia which do not clear away.

Stomatitis.—Some catarrh of the mucous membrane of the mouth is an almost invariable accompaniment of measles. It comes on during the prodromal stage, and passes away with the eruption. It is of importance, chiefly, because it paves the way for secondary infections; the mucous membrane becoming the seat of diphtheria, ulceration, or aphthæ. Ulcerative stomatitis attacks particularly the sulcus between the lips and the gums; but it may be met with on the cheeks opposite the crowns of the teeth. Small, rounded white patches first form, and the necrosed epithelium becomes detached, leaving an ulcer. The destruction of tissue may extend, and by confluence form large elongated ulcers with sharp edges and a purulent or sloughy surface; they may extend to the outer border of the lips, and are then very liable to cause painful cracks and to bleed. The staphylococcus aureus has been found in such cases in almost pure culture. The ulcerations tend to heal as the fever subsides, and are chiefly of importance because the pain they produce tends to make the child refuse food. If neglected, however, they may persist in a chronic or subacute form for weeks or months.

Diarrhœa.—Looseness of the bowels during the prodromal stage is the rule, and diarrhœa of foul, glairy or watery stools may be troublesome about the time the eruption appears. Occasionally the diarrhœa is very copious, and the child passes into a condition of collapse; in such cases the rash is ill-developed or fades, and the case may be mistaken for severe summer diarrhœa. Diarrhœa of a dysenteric character, due apparently to diffuse catarrhal colitis, sometimes occurs, and is very apt to continue as a chronic condition for weeks or months.

Vulvitis.—Inflammation of the vulva with muco-purulent discharge is a frequent complication of measles, and may persist for weeks or months especially in strumous children. The inflammation may go on to ulceration, attended by much pain and swelling of the parts, and smarting on micturition. Occasionally the process becomes exceedingly acute, and leads to brawny induration, and even to gangrene (noma).

Otitis.—Eustachian inflammation is a common complication, and is particularly apt to occur in the subjects of chronic granular pharyngitis and adenoid vegetations. Closure of the tube may be revealed by deafness and tinnitus; but in other cases the symptoms are latent, and the only indications that the inflammation has reached the middle ear are some increase of restlessness, grinding of the teeth, sudden cries, and perhaps delirium. These symptoms, which are commonly attended by a sharp rise of temperature, should lead to a careful examination of the ear. Puncture of the tympanum may give immediate relief. If untreated, convulsions may ensue, or the child may sink into a state of torpor from which it becomes quickly aroused as a purulent discharge from the ear indicates that the tympanum has ruptured spontaneously. Before this happens, however, the mastoid cells may have become infected, or meningitis or thrombosis have been produced. The discharge is foul and very irritating, so that, unless special precautions be taken, excoriation of the external auricle rapidly follows.

Conjunctivitis.—The conjunctival catarrh constantly observed in the acute stage of measles may be very intense, causing great swelling of the lids, and giving origin to a copious sero-purulent discharge. This condition is observed most often in strumous children, and in them phlyctenular ulceration or diffuse keratitis may occur. Occasionally the globe is destroyed by suppuration and rupture.

Gangrene, Noma.—In cachectic children inflammation of some one of the mucous surfaces so commonly involved in measles may take on a peculiar spreading and intense character. This serious complication commonly arises after the subsidence of the eruption, and may with great rapidity produce extensive gangrene and sloughing. This may occur in the mouth or vulva (noma, *vide* "Diseases of the Mouth," vol. iii.), throat, larynx, or ear. It appears to be due to a secondary infection, and is apparently very much less common since the hygienic condition of hospitals, schools, and the dwellings of the poor has been improved.

Renal Disease.—Albuminuria is occasionally observed, chiefly in adults, about the time of the onset of the rash, with which it commonly disappears. It is believed to be due to a temporary congestion, and nephritis is undoubtedly a very rare complication of measles. Chronic albuminuria, with anasarca, has been described as a late sequel of measles, but, to say the least, the connection is not well established.

Serous Effusions.—Ascites, due apparently to subacute simple peritonitis, occasionally occurs as a late complication of measles. It appears to have been chiefly observed in girls. The fluid is eventually absorbed, but may remain for several weeks in sufficient quantity to cause considerable distension of the abdomen. Anasarca is sometimes observed, even though the urine remains free from albumin. Its cause is not explained.

Affections of the Heart.—In a few instances endocarditis has been observed during measles, and pericarditis still more rarely. It is probable that the latter, if not the former also, may be secondary to bronchopneumonia.

The number of cases in which any permanent disorder of the nervous system is produced by measles is small. In spite of the enormous number of children who recover annually from measles, instances of nervous disorders arising in connection with the disease are rare.

Mental Disorder.—A few cases are on record in which the patient, after the fever, remained in a dull, apathetic state. In some there is complete dementia, from which recovery may take place suddenly, as in a case recorded by Casson.

Chorea.—Measles is not generally recognised as one of the common antecedents of chorea; but among the 439 cases of chorea analysed by Dr. Stephen Mackenzie, for the Collective Investigation Committee, there were thirty-two in which measles was the sole antecedent illness; and in seventeen others measles, associated with anæmia, was the sole antecedent illness. On the other hand, measles coming on during chorea generally leads to the diminution of the movements.

Tetany.—In young children, especially in those who have convulsions at the onset, tetany may be observed during the disease, and may persist for some time afterwards.

Hemiplegia.—In 120 cases of hemiplegia in children Osler found four after measles; in eighty cases Gowers found seven after measles. The hemiplegia may come on during the height of the disease, or during convalescence. In most of the recorded cases it has been first noticed after a fit or a series of fits; and in some instances the spasmodic affection has been limited to the side subsequently found to be paralysed. As is the case with hemiplegia coming on during other acute infectious diseases, aphasia exists in a very considerable proportion of the cases. The occurrence of hemiplegia during the acute stage appears to add to the gravity of the prognosis. If the patient recover from the attack of measles very great improvement may take place in the paralysis, though, apparently, not complete recovery. Schwartz has recorded a case of aphasia and paralysis of the extensors of the upper extremity in which both the power of speech and the movement of the arm were completely regained. In the majority of cases of hemiplegia the paralysis persists, and becomes in time associated with arrest of development, of one or both limbs, rigidity, and exaggerated deep reflexes. The pathology of these cases is not very clear; they have been attributed to encephalitis followed by sclerosis, or to localised meningitis.

Muscular Atrophy.—A few cases of limited muscular atrophy, resembling infantile paralysis, are on record as a sequel of measles. They are so few that were it not for the fact that similar lesions occur after other acute specific diseases, the relation might be regarded as one of mere coincidence. Their pathology is very obscure; Dr. Ormerod, who has recorded a series of cases in one family, rejects the theory that they are due to acute anterior poliomyelitis, and appears disposed to associate them with the progressive muscular atrophy of youth.

"*Ascending Paralysis.*"—A rare complication of measles is a form of paralysis which closely resembles in its clinical features that observed after diphtheria. The suspicion that the paralysis is really secondary to latent diphtheria may perhaps have led to some of the cases not being recorded. Barthez and Sanné mention eight cases in which there could be no suspicion of diphtheria. The symptoms in these cases were those of paresis rather than paralysis of the soft palate, the pharynx, the tongue, and of the muscles of the neck; in four cases they appeared during the earliest days of the disease, and in the four others three weeks after. All the patients recovered in from three to twenty days. On the other hand, cases of this nature may terminate in death. The analogy of diphtheria, taken together with the complete recovery which appears to be the rule, lends support to the theory that the lesion in these cases is multiple neuritis. Paraplegia appears occasionally during measles; the reflexes are lost rapidly, the electrical reactions of the muscles are much modified, the patient complains of formication and cramps, and there may be retention of urine and incontinence of fæces. Recovery in from one to six weeks is the rule; but death has been brought about by respiratory paralysis, due apparently to palsy of the diaphragm. Lop attributes these cases to lesion of the cord due to toxæmia.

Disseminated Myelitis.—Disseminated myelitis may arise during the course of measles. This is proved conclusively by Dr. Barlow's case, in which death occurred during the acute stage, and a post-mortem examination was made. In this case the nervous complication came on during the early stage of the exanthem, and such would appear to be the rule. It is in the highest degree probable that the primary lesion was disseminated myelitis in certain other patients who presented, during the acute stage of measles, marked disturbance of the nervous system characterised by stupor, widespread muscular paralysis, and loss of control over the sphincters; and who, after recovery from the acute illness, remained permanently affected by symptoms resembling disseminated sclerosis. In one case which I have recorded, in the *Medico-Chirurgical Transactions* (19), the child was seized with convulsions on the fourth day of an ordinary attack of measles; four weeks later she was in a condition of hebetude, had some difficulty in swallowing, and was unable to sit up, though she could move her limbs feebly. Improvement took place very slowly, and, as she regained power, inco-ordination was a marked symptom, along with coarse tremor on movement. Later, tremor aggravated by intention was present in all the limbs, and involved the head; the deep reflexes were exaggerated. Speech was syllabic. Eventually all the symptoms improved very much; but at twelve years of age she was backward in intelligence, slow of speech, clumsy in movement, and there was some rigidity of the muscles of the limbs and exaggeration of the deep reflexes. It seems highly probable that the disseminated myelitis is due to a specific toxæmia; and this view is confirmed by the fact that the changes found in the cord in Barlow's case were clearly vascular in origin.

Measles and Pregnancy.—A pregnant woman is rarely attacked by measles, but it does not appear that pregnancy confers any immunity. Abortion or premature delivery is apt to occur either during the eruptive stage or at the onset of the prodromal symptoms. Severe hæmorrhage may occur after delivery. Measles very rarely occurs in the lying-in period after delivery. The prognosis of measles in a pregnant woman is good. The chief dangers are—(i.) that broncho-pneumonia, if it occur and the uterus be not emptied, may cause great embarrassment of the respiration; (ii.) that, as the systemic infection of measles appears to dispose to septic processes, the patients may be rather more liable to puerperal septicæmia. On the whole it is desirable to advise a pregnant woman who has not already suffered from measles to avoid contact with infected persons.

Diagnosis.—A well-marked case of measles can hardly be mistaken for anything else. Mild cases may be difficult to distinguish from German measles (*vide* p. 117). The fine red rash which sometimes precedes the true eruption, owing to its resemblance to the rash of scarlet fever, may cause some hesitation. The history of exposure to infection (if it can be obtained), the presence of coryza and photophobia, and the milder degree of throat affection, will probably lead to a correct diagnosis; but in doubtful cases it is wiser to suspend judgment, and to isolate the case as though it were scarlet fever. A discrete eruption, especially if, as is sometimes the case, there be complaint of pain in the back, may cause the case to resemble varioloid; though the converse mistake has probably been more often made. If the character of the eruption be not conclusive, reliance must be placed mainly on the history and the symptoms of catarrh. Acute, widespread dermatitis ("acute eczema") may present considerable resemblance to measles, and herein mistakes have been made even by experienced physicians. Careful examination of all the circumstances of the case will generally prevent error: on close examination the rash will be seen to differ from that of measles, and as a rule areas will be found, most likely about the neck or behind the ears, where the surface is weeping or covered by thin crusts; there will probably be no coryza or photophobia, and the temperature will not be so high as would attend so extensive an eruption were it that of measles. The only safe course in all doubtful cases is to decline to give a positive opinion on the first occasion of seeing the patient. As a rule a few hours' delay will make a decision possible.

The prophylaxis of measles presents special difficulties owing to its extreme infectiousness before the symptoms are characteristic. Personal intercourse, especially in schools, is the main factor in disseminating the disease. Körösi gives statistics from Buda-Pesth which show a remarkable diminution in the number of cases of measles during the three months which include the autumn holiday; and a rapid increase commencing about a month after the schools resume.

It is only, therefore, by dealing with the early cases that the spread of an epidemic in a susceptible population can be controlled. The slight importance which the public is disposed to attach to measles creates a great difficulty. Much difference of opinion as to the value of compulsory notification exists among medical officers of health. It is argued that the fact that many cases are never seen by medical men must greatly diminish the good results to be expected from notification; and, further, that the want of means to isolate patients, and to keep under observation susceptible children who have been exposed to infection, must prevent the application of any effectual measures by a public health authority. On the other hand, the receipt of notifications would be the best guide to a public health authority in deciding whether infant schools should be closed. In face of a commencing epidemic such a step seems certainly desirable; not only because infant schools may be assumed to contain a large proportion of susceptible children, but also because the mortality in the early years of life is much higher than among elder children. Further, early knowledge of an epidemic will enable public health authorities to give parents good advice, to which it is possible that they may after a time be disposed to give ear; and also to supply school authorities with the names of houses or localities in which cases have occurred, so that children from these places should be excluded from the schools. Compulsory notification, it must be confessed, has not hitherto been a very successful means of checking epidemics of measles; but this failure may in part, at least, be attributed to the fact that it has never yet been enforced over an area sufficiently extensive. It is of little use to apply the Infectious Disease Notification Act in a town if it be not also enforced in the suburbs. Further, if the best results are to be obtained, it will be necessary to insist upon the provisions of the Act requiring notification by householders, which hitherto have been very generally a dead letter.

Treatment.—*The prevention of complications* is the most important part of treatment. Its two main elements are cleanliness and ventilation; but it is advisable to keep the child in bed from the onset of symptoms until desquamation is over; or, if this be not noticeable, for a week or ten days altogether. The danger of exposure to cold has been greatly exaggerated. Vierordt recommends that on warm, sunny, still days the child should be rolled out of doors in its bed; care being taken to guard the eyes from light. Great variations in the temperature of the room or exposure to direct draught should be avoided. In cold weather the temperature of the room should be kept at about 66° F., and the air, if necessary, moistened artificially by the steam from a boiling kettle, or by evaporation from an open dish over a spirit lamp. The use of a steam spray presents the advantage that some aromatic disinfectant may be added from time to time to the water, which will at least have the effect of correcting the peculiar acrid, musty odour generally noticeable in a room in which a case of measles is being nursed. In a private house it is a good plan to use two adjoining rooms—the one by day and the other by night; each room while not in use should be cleaned, dusted with a damp cloth, and thoroughly ventilated. Dust and smoke should be avoided, as they tend to increase the irritation of the mucous membrane. Dryness of the air not only increases this irritation, but also favours the dissemination of dust and microbes. The broncho-pneumonia is undoubtedly communicable; and it is undesirable to nurse a child suffering from this complication in the same room with others, or to employ the same drinking utensils. The windows of the room should be shaded by day sufficiently to relieve the photophobia—too dark a room not only has a depressing effect upon the patient, but prevents accurate observation of his condition.

Since the microbes associated with broncho-pneumonia are found to be present in the mouth in more than half the cases of measles, the use of antiseptic mouth-washes is indicated, and the practice appears to have been attended by good results. For this purpose a solution of boric acid (1 to 2 per cent) is suitable, and its use is not ungrateful to a patient old enough to employ it. In infants the solution must be used with a spray or syringe, and, in epidemics in which a special liability to ulcerative stomatitis or to diphtheria is noticed, the employment of antiseptic mouth-washes should be considered obligatory. Further, all precautions designed to prevent secondary infections of the respiratory system should be carried out with particular care in children who by reason of their tender age (six months to six years), or because they are the subjects of rickets or tuberculosis, are specially liable to respiratory complications of a severe type.

Mild cases of measles of the ordinary type do not call for any treatment beyond the observation of the above precautions. No drug is known to have any power in antagonising the specific process. The patient should be fed simply; and the greater the fever and the more severe the type of the disease, the more simple should be the diet. The liability to the occurrence of diarrhœa should be borne in mind, especially in epidemics in which this complication is frequent, or in hot weather, or in individuals disposed to intestinal catarrh. In a robust child a diet of milk and gruel is the best; but in weakly children it may be desirable from the first to give eggs, meat juices, and perhaps small quantities of wine or brandy. The child suffers intensely from thirst, and it may be allowed to take freely of bland fluids, water flavoured with lemon juice or raspberry syrup, or a phosphoric acid drink containing 1 or 2 per cent of phosphoric acid and a little syrup.

Nervous symptoms, if accompanied by high fever, restlessness, and slight delirium, should be treated by keeping the patient lightly covered, and by the application of cold compresses, an ice-bag to the head, or even cold affusion. Sleep may often be induced by applying a cool, moist compress to the trunk, or, in adults, by a pack to the limbs. Much relief is often afforded by rapid washing of the whole body with water or with water and vinegar. When the cerebral symptoms are more severe, especially when there is high delirium with rapid pulse and flushed face, the best treatment seems to be hydropathic, applied either by means of cold or cool packs, or by a short lukewarm bath (90° to 96° F.) A cold affusion to the head, during the bath or otherwise, will increase its calming effect. If necessary, such baths may be repeated several times a day, but the water should not as a rule be used below 82° F.: they will be found to exercise a considerable influence upon the temperature in children. Prostration need not be considered a contra-indication of hydropathic treatment, which on the whole is perhaps best applied by the use of packs, not necessarily of cold water. If the depressing effect of the packs is likely to be excessive, it may be diminished by adding brandy to the water in which the cloths are wrung. Every case must be treated upon its own merits; and it is prudent for the medical attendant himself to watch the effects of the hydropathic treatment, at any rate on the first few occasions of its application. In severe cases with continuous convulsions the action of the bath treatment or of the cold pack is uncertain: sometimes it appears to determine a fresh accession of convulsions; but, before abandoning it in serious cases, it is desirable to try the effect of cold affusions to the head. When there is great congestion of the face, pointing to general cerebral congestion, the application of leeches to the temples or mastoid process may give relief; but before applying them it would be well to try the effect of a cool affusion to the head, the trunk and limbs being wrapped up in a blanket. Severe headache may be relieved by the same mode of treatment, or, except in young children, by the application of a mustard poultice to the back of the neck. Constipation, which frequently attends the cerebral symptoms, should be treated by copious cool enemas, with or without the addition of castor oil. When relief has been obtained by hydropathic measures the packs or baths may be repeated at longer intervals, and their use may be associated with certain antipyretic drugs: of these the most valuable is quinine. The dose of the sulphate may be roughly estimated at about a grain three times a day for each year of the child's age, with a maximum for adults of twenty-five to thirty grains in the day. When diarrhœa is present Vierordt recommends tannate of quinine in doses about three times as great as those of the sulphate; it has the further advantage of being less bitter and more readily taken (in powder) by children. Bromide of potassium has been strongly recommended by Barthez and Sanné in high fever with marked congestion of the head or lungs, and in convulsions. Small doses of chloral may be of use when there is much excitement, irritability, and loss of sleep at the commencement of the disease; but if there be signs of weakness of the heart this drug should be used with care, or avoided altogether; the same remark applies to antipyrin. The last-named drug, however, will sometimes give good results when the fever is high at the onset, with much excitement and sleeplessness: it may be given either in three doses during the day, or in one dose in the afternoon; when it will sometimes procure sleep. The maximum quantity which a child under twelve years of age should receive in a day ought not to exceed eight grains; and in all cases in which there are signs of cardiac weakness it is better to avoid internal antipyretic remedies altogether, or to give only quinine. In cases of the typhoid and asthenic form hydrotherapy is not contra-indicated, but should be used with discrimination. Henoch recommends hot baths or mustard baths, with simultaneous cold affusions to the head. Alcohol is a most useful drug to use in these cases in combination with the cold water treatment; it is a good plan to give a dose of good brandy or whisky a few minutes before a bath or the application of a fresh pack. Vierordt, who herein seems to reflect current German practice, strongly recommends in serious cases with marked heart failure the subcutaneous injection, whenever the pulse fails, of a solution of camphor in oil (1 in 10; or for children under three years 1 in 20). From $\frac{1}{3}$ grain to $\frac{2}{3}$ or $\frac{3}{4}$ grain may be given in this way to a child of two to three years of age. The hypodermic injection of caffein under similar circumstances may also give good results. The dose should be two to three grains dissolved with an equal quantity of benzoate of soda in sterilised water. In children about puberty and in adults strong coffee may replace the use of caffein. Severe hæmorrhagic measles must be treated on the same principle as the typhoid form, but the results are exceedingly unsatisfactory.

Itching of the *skin*, which is sometimes very distressing, may be relieved by local rubbings with carbolic vaseline ointment. During desquamation warm baths should be used, taking special precautions to avoid giving cold. One or two baths with soap and water should be given at the end of convalescence, before the patient returns to other children. *Epistaxis* does not call for special treatment except when very copious or continued. When not severe it will generally be readily stopped by the injection of hot water. If inspection shows that the bleeding comes from the front of the nose the anterior part of the nose may be plugged with antiseptic wool smeared with some antiseptic ointment. The posterior nares ought only to be plugged as a last resource, as the plug quickly becomes extremely foul, and may determine severe pharyngitis or set up acute otitis media. *Laryngitis*, if severe, may be treated by frequent short inhalations of steam or by the pulverisation of a one per cent solution of boric acid or common salt, and by the application of an ice-bag to the front of the neck. The patient should be encouraged to check the cough, and will be assisted by the use of a linctus containing a small quantity of morphine or codeine. Attacks of *paroxysmal cough*, or *laryngismus stridulus*, will be relieved by very hot compresses, applied every ten or fifteen minutes until the skin is very red. Sometimes in young children much relief is obtained by the application of one or two leeches above the manubrium sterni. *Bronchitis* or *broncho-pneumonia* must be treated upon the general principles which guide the management of these disorders when they occur independently of measles. The reader is referred to the chapters on these subjects for further information. The same remark applies to *diarrhœa*, which is sometimes extremely troublesome.

Much may be done to prevent the occurrence of *otitis*. In addition to the use of the antiseptic mouth-washes and gargles already mentioned, the nose and naso-pharynx should be cleansed with a warm solution of boric acid and borax, introduced into the nose by means of a coarse spray or by the gentle use of a syringe. This should be followed by the application of an antiseptic ointment with a camel's hair pencil. The child, if old enough, should be encouraged to blow its nose. In younger children, and in all cases in which deafness, or tinnitus, is present, the use of Politzer's bag, which clears the nose and naso-pharynx and the orifice of the Eustachian tube, has been recommended; but it seems to be open to the objection that infective material may thus be forced into the middle ear. Politzer, indeed, maintains that there is merely a condensation of air in the tube and tympanum, not a transference from the naso-pharynx to the drum-cavity: however this may be, I am indebted to Dr. Dundas Grant for the observation that the risk is abolished or greatly diminished if the naso-pharynx have been previously cleansed, in the manner described above. In his opinion the occurrence of pain in the ear is an indication that only the very gentlest inflation should be used. In such cases relief may be obtained by the instillation of a few drops of a warm watery solution of cocaine and atropine (2 to 3 per cent). If pain or deafness persist, or if inspection of the tympanic membrane show marked congestion, puncture may give relief; and this operation ought certainly not to be delayed if pus be detected bulging the membrane forward. The wound made by the knife heals quickly. In some cases inflammation of the lymphatic glands below the ear may be associated with the ear disease; after the ear itself has been properly treated, belladonna fomentations over these enlarged glands will assist in preventing suppuration. After the subsidence of the acute inflammatory disturbance, Politzerisation and attention to the naso-pharynx are called for if deafness persist. Otorrhœa is best treated by the insufflation of powdered boracic acid.

During convalescence the patient should be fed well, dressed warmly, and guarded from draughts when perspiring. It is not advisable as a routine measure to recommend change of air, especially in the winter, until three or four weeks at least after the disappearance of the rash.

DAWSON WILLIAMS.

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D. W.

RUBELLA

Synonyms.—*Rubeola notha, German measles, Epidemic roseola ;*
Ger. *Rötheln ;* Fr. *Rubéole.*

Rubella, or German measles, is a specific, infectious, eruptive fever, characterised by a long period of incubation, slight prodroma, a rose-red papular rash of short duration, pharyngitis, and adenitis.

At the present time it is not possible to give an altogether satisfactory description of the epidemic disease to which the name German measles is commonly applied in this country. The existence of such a disease is denied by some authors (1), who would refer all the cases either to measles or to scarlet fever; while others believe that under this name are included two or more acute specific disorders, distinct from measles and scarlet fever and from each other. The view, at one time prevalent, that the disease is a hybrid of measles and scarlet fever appears now to be abandoned.

There seems, in fact, to be little reason to doubt that an acute specific disorder, usually presenting symptoms not unlike those of measles but sometimes more nearly resembling those of scarlet fever, does occur at irregular intervals in epidemics of limited extent; and that this epidemic disorder does not afford any protection against measles or scarlet fever.

Ætiology.—The sufferers, as a rule, are children, mainly between the ages of five and fifteen; and the sexes are equally liable. The disease has been chiefly observed in the northern temperate climates; especially in Germany, Great Britain, and the Northern States of America. It appears to be rare in France and Italy. It has been said to be more common among the poorer classes, but this opinion is probably erroneous. Epidemics are not infrequent in public schools in this country. In England and Germany the disease is most prevalent in the spring and early summer; but in America, it is said, in winter and spring. The disease is commonly contracted by personal intercourse; there is indeed no clear evidence that the infection can be retained by fomites.

The incubation period is not well determined. The interval between exposure to infection and the appearance of the rash is probably most often seventeen or eighteen days; but it may be two or three days more, or five, or even, perhaps, seven days less. A patient who has contracted the disease is capable of conveying the infection to others two or three days before the rash appears—that is to say, while he is himself quite free from any obvious symptoms of illness. The capability of infecting others remains during the presence of the rash, but declines rapidly, and in mild cases disappears in a week; though it may persist a little longer after more severe attacks, or, perhaps, when there is much desquamation.

Symptoms.—The prodromal symptoms are slight, and their duration is short, not more than twelve hours; or they may be absent altogether: on the other hand, in the more severe attacks the patient may for two or three days experience malaise, dulness, and headache, accompanied by some suffusion of the eyes, soreness of the throat, slight cough, pain in the back, and glandular enlargement.

Commonly the first symptom noticed is the appearance of a discrete pink papular rash behind the ears and about the orifices of the nose and mouth. Rarely in any case is the appearance of the rash delayed beyond the second day. In rare cases it appears first on the back or chest. It may extend very rapidly to the trunk and limbs, or more slowly—possibly even with distinct intervals, so that there are two or three crops; in either case it may have faded on the chest and face before invading the limbs. The character of the eruption may vary in different cases, and in the same case at different stages. At first it consists only of slightly raised papules, which disappear on pressure, and are of a bright rose-red colour. The spots are lighter in colour, have less defined edges, and are more widely scattered, at any rate at first, than in measles; and they are not arranged in a crescentic manner. The rash in any particular area may begin to fade in a few hours, and fading is seldom delayed beyond twelve hours; but before this occurs the eruption may undergo a marked change, owing to the spread of a bright red flush on the face and neck, while at the same time the limbs become covered by a fine punctate rash indistinguishable from that of scarlet fever. The rash is not accompanied by any itching. The temperature in mild cases rises to 100° or 101° F. when the rash appears, and it falls to the normal about the third day as the rash finally fades. In more severe cases, especially if the catarrhal symptoms of the prodromal stage are well marked, the temperature rises to 100° or 102° F. before the rash appears; going up one or two degrees when the rash comes out. In the rare cases in which serious complications occur the temperature may be maintained at a high level until they subside. The amount of catarrh which accompanies or precedes the rash varies greatly. As a rule there is some sore throat, accompanied often by enlargement of the tonsils; and a general redness of the palate and pharynx has been spoken of as an enanthem: the pharyngeal catarrh is more diffuse, and perhaps, in relation to the temperature and the general condition of the patient, more severe than in measles. The eyes are suffused and water, but there is little or no photophobia. A dry cough may be a source of some discomfort, but is far from a constant symptom. The patient may present some signs of bronchitis, which rapidly pass away as the rash fades.

In the great majority of cases there is little or no depression or sense of discomfort, and the patient may assert that he is perfectly well but for the rash on his face and a certain amount of sore throat. Enlargement of the glands, especially the posterior cervical, those behind the angle of the jaw, and along the sterno-mastoids, is almost a constant symptom: and in some cases those in the axilla and groins will also be found to be enlarged and tender; though, as a rule, the patient makes no complaint. This enlargement of the glands about the neck is always an early symptom, and may be detected as long as a week before the rash appears.

Convalescence commonly begins as the rash fades; the catarrhal symptoms subside rapidly, but the enlargement of the glands may persist for a week or ten days or a fortnight longer. Desquamation does not occur in all cases. According to Dr. Clement Dukes, when the rash is most markedly of the measles type it is commonly very slight and branny, or absent; more copious, but still branny or in small scales, when the rash more nearly resembles that of scarlet fever. A slight rash is commonly followed by slight desquamation; a severe rash may or may not be followed by copious desquamation. The rule is, on the whole, that a severe widespread rash is followed by extensive desquamation, involving even the hands and feet. In mild cases desquamation may be over within a week. In such cases it should be looked for in parts of the person least exposed to friction, especially below the clavicles.

Complications and Sequels.—As a rule rubella runs its course without complications; when they occur they are of the catarrhal type. The angina may be severe and accompanied by the formation of false membranes on the tonsils; swallowing is then painful, and the child's life may be put in danger by the depression and interference with nutrition due to this cause. The bronchitis which sometimes accompanies the rash may be severe and persist after the rash fades, or broncho-pneumonia may appear; pleuro-pneumonia has also been observed as a complication. Slight albuminuria, with some generalised œdema first noticeable about the face, has been observed in a few cases. The pharyngitis has sometimes been accompanied by laryngitis, and by evidences of implication of the middle ear. It would seem that serious complications occur only in cachectic children, or in those specially predisposed to bronchitis and broncho-pneumonia; in them only do chronic coryza and chronic enlargements of the tonsils and glands persist as sequels.

In some epidemics a few cases of **relapse** have been recorded, the intervals varying from a few days to two weeks or even more.

The **Prognosis**, so far as the disease itself goes, is always good, and recovery is usually complete in a fortnight; though, even in healthy children, some general deterioration in health may remain. The only reservation is that in cachectic children, or in those already suffering from some serious chronic disorder, such as tuberculosis, a fatal termination appears sometimes to be determined by an attack of rubella.

Aberrant Forms.—Among the cases commonly classed as rubella there are some, which occur generally in groups, characterised by the absence of prodromal symptoms, by the very mild type of the general symptoms (the temperature being little if at all raised), by the absence of sore throat, coryza, or catarrh, and of enlargement of the lymphatic glands. The Council of the Medical Officers of Schools Association, in a recent circular, suggests that these groups of cases are really examples of an exanthematous disease distinct from rubella. The name "**infectious roseola**" or "infectious rose rash" is proposed as the designation of this disorder. The cases are met with most often in summer, and their characters are thus described in the document:—"The rash appears suddenly, usually with but slight fever, on the neck, limbs, and trunk; its distribution is irregular, and the face frequently escapes altogether. The eruption consists of large rounded areas of bright red, closely-aggregated spots scarcely raised above the surface of the flushed skin. It begins to fade on the parts first attacked as it extends elsewhere, and usually disappears within thirty-six hours, the slight pyrexia subsiding with it. There is scarcely any interference with the general health; the fauces may be slightly reddened, but there is no appreciable sore throat, coryza, or catarrh, and no enlargement of the lymphatic glands."

Dr. Clement Dukes believes that suffusion of the conjunctiva—**pink-eye**—may be the only symptom of an attack of rubella; though the patient may communicate the fully-developed disease to others. He believes also, and there seems to me great probability in the suggestion, that rubella may give evidence of its existence only by producing slight feverishness and some enlargement of the lymphatic glands throughout the body. The suggestion is the more worthy of note as in France, where rubella would appear to be very seldom observed, some writers have described a "glandular fever" in children which is apparently infectious.

Treatment.—An ordinary case of rubella hardly calls for any treatment by drugs. The patient should be kept in bed, much as he may object—and commonly he will object much—until the rash has completely disappeared. Catarrhal complications should be treated as the like symptoms in measles. The patient should be kept in bed for, say, five days; for three or four days more he should be kept indoors; then, while still isolated, he should have as much fresh outdoor air as is possible. Desquamation does not contra-indicate outdoor exercise.

Diagnosis.—In the accompanying table are classified the symptoms upon which reliance must chiefly be placed in making the diagnosis between Rubella, Measles, and Scarlet Fever (2).

	Rubella.	Measles.	Scarlet Fever.
INCUBATION PERIOD	9 to 21 days, usually 18.	5 to 14, usually 10 (14 to rash).	Usually about 2 days.
PRODROMAL SYMPTOMS	Short and slight.	3 to 4 days, generally marked.	Brief: a few hours; rarely 5 days. Very rarely 7 days. Vomiting frequent.
RASH	First or second day, commonly first symptom, rosy-red dots. First, or early, about mouth.	Fourth day. Papular brick-red, or darker and crescentic, appear about mouth or forehead.	Dusky red and often diffuse. Skin burning.
CATARRHAL SYMPTOMS	Redness of throat, diffuse. Conjunctivæ suffused; watering of eyes slight. Bronchitis slight; broncho-pneumonia rare. Diarrhœa absent.	Redness of throat, patchy at first. Catarrhal conjunctivitis. Much lachrymation and photophobia. Bronchitis usually marked; broncho-pneumonia common. Diarrhœa frequent.	Throat affection proportionate to skin eruption. Dusky red. White plugs in tonsillar glands. Conjunctivæ unaffected. Lung complications uncommon. Diarrhœa absent.
LYMPHATIC GLANDS	Generally enlarged, tender, and hard, including posterior, cervical, axillary, and inguinal.	Enlargement not marked early. Generally limited to those about the angle of the jaws.	Enlargement of neck glands proportionate to faucial affection.
GENERAL SYMPTOMS	Little or no depression. Tongue clean or slight fur; appetite often retained. Temp. may be normal. Pulse little altered, or accelerated in proportion to fever.	Depression generally marked, often much prostration. Tongue furred; little or no appetite. Temp. usually 100° or more. Pulse generally accelerated in proportion to fever; often weak and dicrotic.	With much rash much depression. Tongue coated; peeling on fourth day, leaving "strawberry" tongue. Temp. always raised, often 105° to 106°. Pulse always accelerated; commonly out of proportion to fever.
ALBUMINURIA	Rare and slight.	Very rare.	Very frequent.
CONVALESCENCE	Rapid.	Commonly more protracted.	Often prolonged owing to complications.
DESQUAMATION	May be copious; always fine.	Seldom copious; fine.	Generally copious; in shreds.

Prophylaxis.—As the disease is certainly infectious before the appearance of the rash, isolation, to be effective, must be enforced before the disease can be diagnosed with certainty. Practically the only safe course is to separate all susceptible persons who have been exposed to infection from others who have not been so exposed, until the end of the third week after the date of exposure; if at the end of that time they are free from elevation of temperature, from enlargement of the glands, and from sore throat, they may be assumed to have escaped the disease. If this rule be followed, mistakes will very seldom, if ever, be made. As adults—whether because most adults have already suffered from an unremembered attack of rubella, or because the adult age does confer immunity—are little liable to the disease, this quarantine may perhaps safely be relaxed in their case. A patient recovered from rubella should not be allowed to mix with other susceptible persons until three weeks have elapsed from the beginning of his illness, nor until after he has taken a series of general baths to which some disinfectant may be added, though few are superior to soap, especially soft soap. Although there is no positive evidence that infection can be conveyed by clothes, the disinfection of those belonging to the patient appears to be a reasonable precaution. In mild cases, especially in those of the measles type, the period of isolation after an attack, above recommended, may be diminished by a week. Dr. Clement Dukes' experience is that, if disinfection be practised, the persistence of desquamation after the third week need not be held to render further isolation necessary.

DAWSON WILLIAMS.

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D. W.

SCARLET FEVER

SYNONYMS.—*Scarlatina, Febris rubra;* Ger. *Scharlach;* Fr. *Scarlatine, Fièvre rouge;* Ital. *Scarlattina, Febbre rossa.*

I. Historical Survey; Prevalence.—The original habitat of scarlet fever is a matter of uncertainty, although from the earliest records on which any reliance can be placed, and from subsequent data, we are justified in assuming that the disease, at any rate for the past few centuries, has shown a marked predilection for European soil. It is asserted by Collie that scarlet fever existed in the time of Hippocrates, and indeed it has been assumed that the Plague of Athens was a malignant form of the malady, but the interpretation of the cases quoted in support of these opinions may be fairly called in question.

The careful investigations of Hirsch led him to believe that the earliest definite record of scarlet fever dates from the year 1543, and he refers to an epidemic which at that time prevailed in Sicily; it is stated by Haeser that the disease was briefly alluded to in the writings of Ingrassia of Palermo in the year 1550.

In the following century, however, we get upon firmer ground, for clear indications of its prevalence in Prussia during the first half of the seventeenth century is to be found in the writings of Doring and Sennert, and of Winsler and Fehr—although great confusion at that time existed between scarlet fever, measles, erysipelas, and (in all probability) diphtheria. This confusion was recognised by Sydenham, who, it seems, was the first to christen the disease "scarlet fever." His careful description of the disorder, as it prevailed in London during the years 1661 to 1675, not only laid the foundation of an accurate knowledge of its special characters, but at the same time clearly differentiated scarlet fever from measles, with which it had been hitherto confounded. Morton, however, a contemporary of Sydenham, continued to speak of the disease as "Morbilli confluentes," being evidently unimpressed by the distinction.

Sydenham undoubtedly underrated the importance of scarlet fever, and even went so far as to say that it hardly deserved the name of disease; he had evidently never seen it in a severe form, and he makes no allusion to sore throat as a symptom of the affection. This seems all the more extraordinary, when it is remembered that so much confusion has continually existed between the diagnosis of scarlet fever and diphtheria, and, as Hirsch suggestively points out, the confusion of scarlet fever with other forms of throat illness has increased in proportion as the differentiation from measles has been recognised.

Since the time of Sydenham outbreaks of scarlet fever of varying severity have been frequent in this country; and its constant presence, in a more or less sporadic form, in the large towns of Western Europe has not been without its influence on the death-rate.

The continents of Asia and Africa, except in isolated localities, have shown but little tendency to provide a field for scarlet fever, but America has been by no means exempt. The disease seems not to have reached North America until the year 1735, when it first appeared in Massachusetts; from thence it spread over the whole of the New England States, reaching New York in the year 1746. During the latter half of the eighteenth century outbreaks of scarlet fever are reported at irregular intervals in the states lying along the eastern and south-eastern shores of North America. In the year 1791 it penetrated into the interior for the first time, reaching Canada and the Northern States during the early years of the present century.

It was apparently not until the year 1830 that the disease obtained a foothold in South America, since which time it has become generally diffused over the continent, where it often appears in widespread epidemics, characterised at times by considerable malignancy.

According to Hirsch, scarlet fever appeared in Polynesia for the first time in 1848; it arose simultaneously in New Zealand and Tasmania, whence it spread to the Australian continent a few years later.

On carefully surveying the records of scarlet fever epidemics in the past, it is manifest that nothing approaching periodicity has characterised its epidemic prevalence. Epidemics of the disease have occurred at irregular times, often separated by intervals of twenty years or more; but having once obtained a foothold, the period covered by the epidemic has usually extended over several years. Besides an absence of periodicity in the epidemic cycle of scarlet fever, it should also be noted that during the intervals there has not usually been the more or less complete disappearance of the disease, which we see in measles, small-pox, and typhus; but that there has been a tendency for scarlet fever to hang about the locality in a sporadic form, and occasionally, by the aggregation of cases, to constitute a minor epidemic.

The constant presence of scarlet fever in the north-western countries of Europe, and, with certain local exceptions, the equally constant immunity enjoyed by the tropical and sub-tropical regions of Asia and Africa, are as true of the present date as of old. That its comparative prevalence is in no way dependent upon the facilities of human intercourse, is shown by its complete absence in an epidemic form from certain countries which lie along the main routes of traffic throughout the world—such, for instance, as Egypt, India, Burmah, Ceylon, the Straits, China, and Japan, although its importation has been, and is a matter of frequent occurrence. The prevalence of scarlet fever in an epidemic form on the continent of Australia is not common, whereas from the populous districts of North America it is never absent.

Although the epidemic prevalence of scarlet fever in the United Kingdom, or even in any considerable district of it, is characterised by a marked absence of periodicity, yet in many large manufacturing towns, in which the disease is now practically endemic, a tendency has been apparent of late to the recurrence of a regular epidemic extension every few years. This may fairly be regarded in the light of a definite local cycle.

An examination of the death-rate since 1860, when scarlet fever was first tabulated apart from diphtheria, shows that London has been subject to this periodic extension of the disease every five or six years. The relative prevalence of the disease may be fairly inferred from these mortality returns, as the type of attack, at any rate since 1870, has not shown any corresponding fluctuation.

During the last twenty years it appears that the prevalence of scarlet fever in this country has undergone considerable diminution; and the decline has been more or less progressive. There is, however, but small justification for the belief that this improvement will be permanent. Indeed, since 1891 a tendency towards increased prevalence has been manifest in London; but in all probability this is simply an expression of the regular cyclical fluctuation of large towns, and has no connection with those larger epidemic waves which have hitherto affected the country at irregular intervals.

TABLE I.—Average annual number of Deaths from Scarlet Fever per million living in successive quinquennia since the separate tabulation of Scarlet Fever.

Date.	England and Wales.	London.
1861–65	982	1119
1866–70	960	1147
1871–75	759	575
1876–80	680	624
1881–85	436	426
1886–90	241	244
1891	171	140
1892	190	274
1893	235	369

The comparatively greater diminution in the number of deaths in London than in the country at large since the year 1870 is in all probability owing to the relatively large increase in hospital accommodation in the metropolis. The extension of the practice of isolation not only lowers the case mortality, but limits the extension of the epidemic.

The dependence of scarlet fever prevalence upon season is more intimate, and the regularity of the association is most strikingly indicated, both by the records of large towns in which notification is in force, and by an examination of the Registrar-General's death returns since the year 1860. In London valuable evidence of the seasonal prevalence of the disease is afforded by the monthly admissions into the hospitals of the Metropolitan Asylums Board, which now receive over 60 per cent of the scarlet fever cases notified in the town.

These records go to prove that in this country scarlet fever is least prevalent in the months of March and April; after which a slow and steady rise takes place until the mean is passed at some time during the month of August. A rapid extension of the disease occurs in September and October, reaching its climax usually during the last week of the latter month. From the beginning of November the curve shows a steady decline, dropping more rapidly during December until the mean is reached again, either towards the close of that month or during the first two weeks of January (Chart A).

The seasonal prevalence of the disease in London as evidenced by the admissions into the Asylums Board and London Fever Hospitals is practically identical. That the highest point of the curve in the following chart occurs somewhat earlier in October than it does in the foregoing one, is in part due to the fact that it signifies the dates on which the cases came under treatment, not those on which the attacks proved fatal (Chart B).

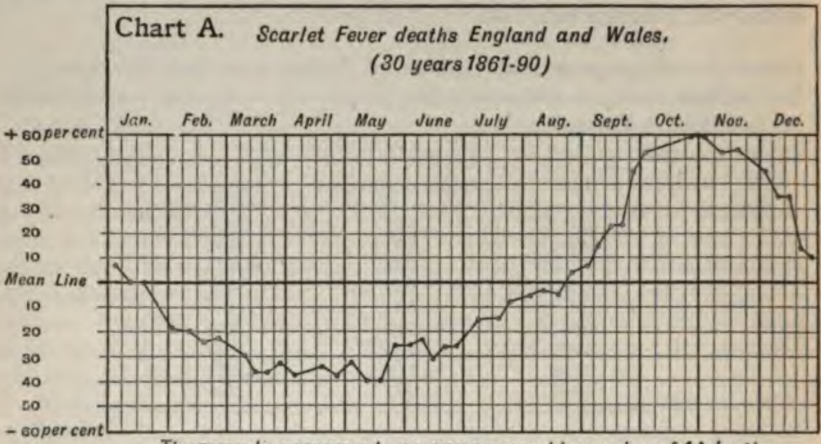
Chart A. *Scarlet Fever deaths England and Wales. (30 years 1861-90)*

The mean line represents an average weekly number of 44 deaths.

It will be seen that the prevalence of scarlet fever is above the mean during the last five months of the year; and that it is below the mean during the first seven. Although this may be taken as characteristic of the behaviour of scarlatina in European countries, it by no means follows

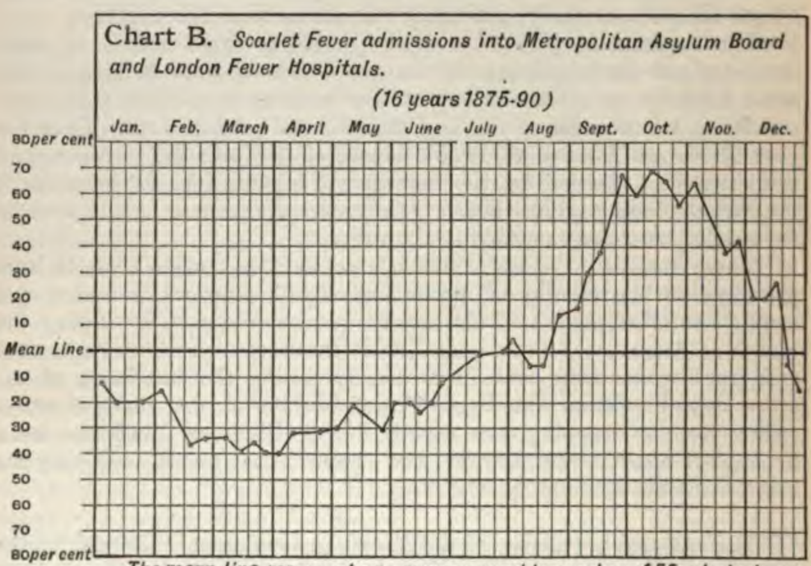
Chart B. *Scarlet Fever admissions into Metropolitan Asylum Board and London Fever Hospitals. (16 years 1875-90)*

The mean line represents an average weekly number of 55 admissions.

that the same holds good for all parts of the world. Indeed, Whitelegge states that in New York the seasonal curve of the disease is entirely reversed; and in Australia, a country in which scarlet fever is by no means widely prevalent, its diffusion is much more variable. The regular seasonal variation of scarlet fever is very suggestive of the operation of some climatic influence; yet it must be confessed that all attempts, and there have been many, to establish any definite association with either temperature, latitude, dampness or soil have been signally unproductive up to the present.

II. **Epidemic Type; Fatality.**—All the records of scarlatinal epidemics in the past go to prove that the fatality of the disease in different outbreaks has been subject to enormous variation; and this opinion is confirmed, up to a certain point, by our own experience at the present day. This variation in fatality is marked, not only in epidemics widely separated both in time and locality, but also in outbreaks which have been simultaneously prevalent in contiguous localities. Moreover, it has been occasionally noticed that the type of attack has undergone a distinct change during the course of a particular epidemic, the usual tendency being for the attacks to become milder towards the close of the outbreak.

The type of the disease may, however, remain constant for many years in a particular locality; this is attested by the writings of Sydenham, who, as it would appear, had never met with a severe case in his own practice. Trousseau, too, reports that Bretonneau had never seen a death from scarlet fever in Tours from the year 1799 to 1822, but that in the year 1824 the disease prevailed in a most malignant form in the town and surrounding district. Graves, again, in describing the Dublin epidemic in 1802, states that the disease at that time prevailed in a very malignant form; but in the following year the type completely changed and a mild character was maintained through successive outbreaks for twenty-seven years, after which the disease resumed its former intensity. The same variation in severity has been found in the epidemics of scarlet fever on the continents of Europe and America; but in Australia it has been more uniformly mild. A notable exception, however, occurred in Melbourne in the year 1874, when the town was ravaged by an epidemic of great malignancy.

Many attempts have been made to trace a connection between the influences of climate, season, soil, and locality and the type assumed by scarlatinal epidemics, but hitherto without success. Hirsch, however, while investigating the type of 265 epidemics in relation to season, found a slight preponderance of severity in the summer and winter months—a result by no means confirmed in this country.

The general mortality has varied, in different epidemics, from 2 or 3 to 30 per cent; and there seems little doubt that the severity of the disease in this country has of late years been gradually diminishing.

Owing to the fact that compulsory notification of scarlet fever has only been widely enforced since the year 1890, it is very difficult to obtain a long and continuous record of the case mortality in any particular district. In London, however, the mortality of the cases admitted into the hospitals of the Metropolitan Asylums Board is of value in arriving at an estimate, as they now receive considerably more than half of the cases annually notified in the town. During the last twenty-three years 81,350 cases of scarlet fever have been treated with a combined mortality of 8 per cent; but since the year 1874 the annual percentage mortality has steadily fallen from 12·2 to 5·9. This reduction of mortality in recent years is no doubt partly due to an improvement in the average social status of the patients received. The latter figure, however, can hardly be taken as representative of the general scarlet fever mortality of London at the present day, as the cases sent into hospital include the larger proportion of severe attacks.

A comparison of the number of deaths with the number of cases notified in the town, the only method for which complete accuracy can be claimed, shows that during the last few years an actual reduction in the case mortality has occurred.

Table II.—Showing the Scarlet Fever Mortality in London calculated from Notifications and Deaths, and that in the Hospitals of the Metropolitan Asylums Board during the last five years.

Year.	Notifications.	Deaths.	General Mortality.	Hospital Mortality.
1890	15,330	876	5·71	7·86
1891	11.398	589	5·17	6·67
1892	27,095	1174	4·33	7·28
1893	36,901	1596	4·32	6·11
1894	18,440	962	5·21	5·92

The general case mortality of scarlet fever in London at the present day would therefore appear to be about 5 per cent. Although the severity of scarlatinal epidemics in the past has by no means always varied in direct relation with the social status or environment of its victims, nevertheless it is a matter of common observation that the disease affects with greater severity the inhabitants of those overcrowded districts of London in which poverty is rife and ill-nutrition common, than it does the more affluent classes living in the comparative luxury of the west end and more open parts of the town. The aggregate type of attack in large towns is for this reason a very mixed one. Constancy of type is best seen in rural districts and amongst the inmates of large institutions. An epidemic of scarlet fever arising in a school or orphan asylum, or amongst the employés of a club or large business house, is usually extremely mild, either in virtue of a healthy régime or the favourable age of its victims. (For the personal factors influencing the case mortality, see Prognosis.)

III. Spread and Infectivity.—The contagious element of scarlet fever is always derived from a previous case; in most instances by the direct inhalation of the breath, or of air charged with minute particles either of shed epithelium, or of the desiccated discharges from some mucous cavity. That scarlet fever is not spread to any distance by aerial convection is well shown by the negative experience derived without exception from certain large fever hospitals, whose walls are closely surrounded with small tenements, for the most part crowded with young children.

The possibility of scarlet fever being transmitted by means of the urine in cases of chronic albuminuria must be admitted; but its actual occurrence is certainly not supported by experience.

The virus may be conveyed by means of various articles which play the part of fomites. Many instances have occurred in which the agency of books, clothes, toys, furniture, bedding, parcels and letters, as vehicles of contagion, has been clearly indicated. Such articles are capable of retaining the contagion in a potentially active form for long periods; certainly for two years, and possibly for more, under such favouring conditions as aerial stagnation, moderate temperature, and the absence of daylight.

In certain rare instances it would seem that the contagion has been transmitted by a doubly indirect method,[1] and the possibility of linen in the laundry becoming infected by that of a scarlet fever patient must always be remembered. Even at disinfecting stations the servant who receives the articles for the stove is not uncommonly engaged also in their removal from it.

Scarlet fever is sometimes widely disseminated by means of an infected milk-supply, and this mode of diffusion has been frequent of late years. Until the now historic outbreak in Marylebone, in the year 1885, it was universally believed that in these milk epidemics the milk was specifically contaminated from a human source—either directly from the hands of the milker, or from accidental exposure to the products of a case of scarlet fever at some point of its transit between the cow and the consumer. The careful investigations of Messrs. Power and Wynter Blyth in the outbreak referred to led them, however, to disregard the possibility of the milk having received its infective properties from any human source. The milk was known to have been supplied from a dairy-farm at Hendon, and, further, it was definitely proved to have been exclusively derived from certain cows which were suffering from a peculiar disorder. Dr. Klein, as a result of careful research, came to regard this disease in the Hendon cows as the key to the epidemic in Marylebone, and the evidence he adduces undoubtedly lends confirmation to the belief that it was the analogue of human scarlatina. (See Pathology.)

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[1] Dr. Caiger wishes me to refer here to a case which occurred in my own practice. The facts are that a father staying in the house of a friend met, on the platform of a railway station thirty miles away, his son who came to this station from a school in which scarlet fever was then prevalent. The two spent an hour and a half together and then returned to their respective quarters. Within the next four days the lady of the house to which the father returned fell ill and died of malignant scarlet fever. The father and the son remained well. Although the father made anxious efforts to find the cause elsewhere, no source of infection other than that which suggested itself could be discovered.—Ed.

If it be ultimately established that the lower animals are capable of developing the disease and transmitting it to mankind, it is evident that our views of the epidemic possibilities of scarlet fever must be correspondingly extended. Moreover, if Klein's teaching be confirmed, viz. that scarlet fever and the Hendon cow disease, though showing considerable variation in their clinical appearances, are due to one and the same micro-organism, it lends support to the statement of Thomas, that a disease corresponding to human scarlet fever has been met with in horses, dogs, cats, swine, and other domesticated animals. Without going so far as to deny the possible truth of this statement, I am convinced, by a somewhat extensive experience in this direction, that cats, at any rate, rarely, if ever, actively convey the infection of scarlet fever.

Scarlet fever has been successfully inoculated into children by several observers in Germany, but the method has no bearing on the spread of the disease.

The scarlet fever patient is capable of imparting infection from the very commencement of his illness; but the time at which his infectivity ceases is not only very difficult to determine, but probably varies widely in different cases. It is a good rule in practice to regard six weeks from the rash as the minimum length of quarantine; after this, the patient's release will be dependent upon the end of peeling, and upon the cessation of any discharges from the ears, nose, eyes, a mucous cavity, or wound of any description. An otorrhœa may certainly retain infection for a period of six months, even if it have been present before the scarlatinal attack; and the desquamation, though usually complete in six or eight weeks, may persist and be contagious for a period of three or four months. There is no reason to regard the second peeling, which occurs in some cases, as necessarily infectious, though there is every reason to regard that which follows a definite relapse of the disease as being no less a source of danger than the original peeling. Redesquamation is in most cases confined to the hands and feet. The patient is most infectious when the disease is at its height, and at the decline of the febrile stage, when a fine powdering is noticeable on the face and other parts. As convalescence advances the degree of infectivity attaching to the cuticle progressively diminishes. The popular belief on this matter is erroneous.

A certain proportion of the cases discharged from a fever hospital, perhaps two or three per cent, seem to communicate the disease to other members of their households on their return, in spite of the most scrupulous care in their final disinfection. It is possible that the respiratory tract may remain charged with infection for several days after a person has ceased living in an infected atmosphere, and as we are unfortunately unable to make sure of thoroughly disinfecting the air-passages of a living person, it is wise to warn the patient against the possible risk of a too free intercourse with other members of his family for several days at least after his return home. In spite of every precaution these so-called "return cases" will occasionally appear.

IV. Individual Susceptibility.—This, in respect to the contagion of scarlet fever, will be found to vary with age, sex, state of health, idiosyncrasy, and previous attack. Of these strictly personal factors the first and last are undoubtedly the most important.

Age.—During the first year of life the liability to scarlet fever is not very great; but from the time of birth it shows a rapid increase until the maximum is reached during the fifth and sixth years. From this time onwards a progressive diminution of susceptibility sets in, which is continued throughout life. On reference to Table III., which deals with the age incidence of nearly 70,000 cases of scarlet fever treated in the Hospitals of the Metropolitan Asylums Board, it will be seen that nearly three-sevenths of the whole number fall within the second quinquennium of life, and nearly two-sevenths in the first; the remaining two-sevenths are distributed in the later quinquennia, of which the third claims considerably more than half. It will be evident, therefore, to what an extent early youth determines susceptibility to the disease.

TABLE III.—Showing Incidence of Age, Sex, and Mortality of 69,752 cases of Scarlet Fever admitted into the Hospitals of the Metropolitan Asylums Board from 1871 to 1893 inclusive.

Ages.	Males.			Females.			Total.		
	Cases admitted.	Died.	Mortality per cent.	Cases admitted.	Died.	Mortality per cent.	Cases admitted.	Died.	Mortality per cent.
Under 5	9,767	1834	18·8	9,825	1741	17·7	19,595	3575	18·2
5–10	13,637	797	5·8	15,126	801	5·3	28,763	1598	5·6
10–15	5,759	144	2·5	6,585	173	2·6	12,344	317	2·6
15–20	2,214	70	3·2	2,477	60	2·4	4,691	130	2·8
20–25	932	22	2·4	1,312	40	3·0	2,244	62	2·8
25–30	390	17	4·4	667	20	3·0	1,057	37	3·5
30–35	240	12	5·0	348	15	4·3	588	27	4·6
35–40	92	8	8·7	167	7	4·2	259	15	5·8
40–45	53	5	7·7	65	3	4·2	118	8	5·7
45–50	17	...		31	1		48	1	
50–55	16	1		15			31	1	
55–60	4	1		3	...		7	1	
And upwards	1	...		6	1		7	1	
Totals	33,122	2911	8·8	36,630	2862	7·8	69,752	5773	8·3
Cases under 5 years of age admitted during the years 1888 to 1893.									
Under 1	224	63	28·1	194	66	34·0	418	129	30·9
1–2	773	203	26·3	728	200	27·5	1501	403	26·8
2–3	1429	309	21·6	1482	328	22·1	2911	637	21·9
3–4	2106	344	16·3	2095	299	14·3	4201	643	15·3
4–5	2355	261	11·1	2447	258	10·5	4802	519	10·8
Totals	6887	1180	17·1	6946	1151	16·6	13,833	2331	16·8

Sex.—The influence of sex is not very great. Females are attacked more frequently than males in the proportion of about eleven to ten. This preponderance in respect to female attacks is seen at each quinquennium, but at ages under five years the disparity is less marked.

State of Health.—The liability to scarlet fever is considerably increased by the presence or recent attack of any other acute disease; and to this rule the other members of the infectious group are certainly no exceptions [see "Coexistence of Infectious Diseases"]. The liability is in all probability greatest in a person suffering from diphtheria. It is very doubtful whether a strumous, tubercular, or other dyscrasia augments in any way the susceptibility to scarlet fever; although a predisposition is certainly engendered by the presence of any form of catarrh, especially if localised in the fauces. The proneness shown by the inmates of a children's ward to take the infection of scarlet fever is a matter of common observation, and the almost uniform mildness of its manifestation has given a special significance to the term "Surgical Scarlet Fever." That a woman during her puerperium is thereby rendered more susceptible to the contagion of scarlet fever than she would have been if subject to any other lowering influence is at least doubtful. Although I am by no means convinced of the truth of the assumption, I would regard the development of scarlet fever in a puerperal woman with the greatest anxiety.

Idiosyncrasy.—The immunity enjoyed by some individuals who, though frequently exposed to its infection, have never at any time been attacked by the disease, is a curious fact. In some instances this immunity is shared by all the members of one family, and in certain cases would appear to be hereditary. Of the conditions regulating it, however, we have absolutely no knowledge. Experience shows that we are not justified in regarding such immunity as necessarily lifelong. Upon other families the disease seems to fall with peculiar severity.

Previous Attack.—The acquired immunity conferred by one attack in most cases persists throughout life; but second attacks of scarlet fever, arising some years after a previous one, are occasionally met with in persons in whom the genuineness of the primary attack was beyond dispute. (See "Complications of Scarlet Fever—Relapse.")

V. Incubation.—In the large proportion of cases in which it is possible to define the length of incubation with any degree of accuracy, the period between a single definite exposure and the first appearance of the febrile symptoms has been either two, three, or four days. In some well-authenticated instances the latent stage appears to have been less than forty-eight hours, but not much less. It is a significant fact that in some of those cases for which an incubation period of less than twenty-four hours has been claimed, the rash has not appeared until the third or fourth day of the recorded attack; the early sore throat with which the attack was dated may not have been a symptom of scarlet fever at all; a simple tonsillitis or faucial catarrh seems to render a person distinctly more susceptible to the action of the scarlatinal virus.

On the other hand, the period of incubation is sometimes as long as five days and, in rare instances, even six. It is sometimes loosely stated that the latent stage in scarlet fever may extend to the length of a fortnight or more, but such statements must be received with caution. I have never met with an instance in which there was any valid reason to believe that the period had been longer than six complete days. The point is one of practical importance to parents, schoolmasters, and other persons concerned with the custody of children. To them it may be confidently stated that, if the first case was properly isolated and the necessary measures for disinfection scrupulously carried out, the safety of the other members is practically assured if no second case have arisen before the end of a week.

VI. Invasion.—The scarlatinal attack in most persons develops itself with considerable rapidity. In addition to the ordinary signs of the febrile state—such as chills, weariness, aching pains, coated tongue, loss of appetite, broken rest, etc.—there are three symptoms which, in the frequency of their observed association, are eminently suggestive of commencing scarlet fever. These are sore throat, headache, and vomiting; to these may be added, less decidedly, diarrhœa. Of these, sore throat accompanied by more or less submaxillary tenderness and a variable degree of painful deglutition, is probably the most constant: next to this, in adults, headache is the most frequent symptom. In young children vomiting is relatively more frequent than headache: diarrhœa, too, more commonly occurs in children, especially on the approach of a severe attack. An analysis of 1008 consecutive cases, in which the history of onset was inquired into, showed that vomiting occurred in no less than 80 per cent. In this series more than 75 per cent of the patients were under 10 years of age.

I have said that in a certain number of cases a sore throat may have preceded the other symptoms of invasion by several days, even a week. But in them a distinct aggravation of the throat symptoms is usually seen when the rise of temperature, vomiting, headache, and other signs of acute invasion supervene: the early sore throat was probably unconnected with the attack of scarlet fever, or but a disposing factor.

As a general rule severity of initial symptoms implies severity of attack, especially in respect to persistent vomiting, which is the rule in cases of the toxic variety. Some very mild cases exhibit a complete absence of prodromata; the rash may be the earliest and most prominent sign of illness.

VII. Clinical Varieties.—Although no fast line can be drawn between one form of attack and another, yet for the purposes of clinical classification, and more important still, in reference to prognosis, cases of scarlet fever can generally be referred to one or the other of the three following classes—

(1) Simple; (2) Septic; (3) Toxic.

Of these the two latter are by far the most grave. It must be remembered, however, that individual cases vary much in the severity of their manifestations, and insensible gradations are seen on the confines of these classes.

1. *Simple Scarlet Fever.*—Otherwise known as Scarlatina Simplex or

Scarlatina Benigna. A case of this, the most common variety, may be expected to conform to the following brief description:—After the symptoms of invasion have persisted, usually with moderate severity, for about twenty-four hours, the characteristic scarlet eruption appears, being in most instances first seen on the neck and chest. In a considerably smaller number of cases the rash may be delayed even as long as thirty-six hours after definite invasion. It is attended with an aggravation of the throat symptoms, and the tongue becomes thickly coated. Faucial discomfort and more or less difficulty in swallowing are complained of, the attempt being attended in some cases with severe pain running up into one or both ears. Tenderness and a slight but palpable fulness of the submaxillary lymphatics are present in almost every instance. Along with the increase in faucial discomfort the rash continues to extend, the pulse to increase in frequency, and the temperature to rise, until a climax is reached on the third or fourth day of illness, by which time the tongue presents the characteristic strawberry appearance. Then, or a day later, defervescence sets in attended with a gradual improvement in all directions; the temperature and pulse steadily subside, the eruption fades, the throat symptoms abate, and convalescence is reached on the sixth, seventh, or eighth day unless interrupted by some complication. It may therefore be stated that the febrile stage of simple scarlet fever lasts about a week, and even before this time some peeling is usually to be found in certain situations.

2. *Septic Scarlet Fever.*—This form of attack, often designated Scarlatina Anginosa or Scarlatina Ulcerosa, most commonly affects young children. It is characterised by an ulceration, which, though invariably commencing in the tonsils, may by its extension lead to widespread destruction of the neighbouring parts. The process is attended with the gradual development of the symptoms of septicæmia. Briefly, the course of the attack is as follows:—After the signs of invasion (which are usually more pronounced than in the previous class of case) have persisted for some twenty-four hours more or less, the eruption appears. It is usually intense and somewhat dusky, often patchy in its distribution, and usually shows a tendency to staining, which may go on to the formation of definite petechiæ; with the development of the rash the temperature rises rapidly, and by the third or fourth day may reach 104°. The tonsils are much swollen and the faucial mucous membrane acutely inflamed. The surface of the tonsils often presents necrotic patches of variable extent, or the tonsils may be covered with an exudation which is very likely to be mistaken for concurrent diphtheria [see "Coexistence of Infectious Diseases"]. The tongue by this time will probably present the characteristic strawberry appearance. From this point the condition, instead of beginning to amend as in simple scarlet fever, continues with undiminished severity. The temperature remains high, and is of an irregular, remittent character. The exudation or superficial slough, if present on the tonsils, gives way to definite ulceration, attended with progressive infiltration of the subjacent lymphatic glands and surround-

ing cellular tissue. This brawny infiltration of the tissues of the neck is most distinctive of septic scarlet fever, and if developed on both sides, may completely encircle the neck like a collar. A profuse muco-purulent discharge escapes from the nares, which become more or less blocked in consequence. In some cases the discharge is thin and sanious, and by its irritant effect excoriates the skin surrounding the nostrils. By the end of the week the tongue again becomes coated and dry, and the breath offensive. During the course of the second week, unless improvement set in, the patient's state is usually aggravated by further changes. The temperature becomes of a more septic character, showing diurnal variations of two or even three degrees; and the pulse more rapid and feeble, being in young children often over 160. Deglutition becomes more difficult, or, in consequence of progressive destruction of the parts, even impossible. Thus food and offensive secretions may enter the larynx, and bronchitis or broncho-pneumonia result. The condition of the patient at this juncture is deplorable in the extreme. Any attempt to swallow is attended with the passage of food into the nares. Sleep is impossible in consequence of the entrance of irritant secretions into the larynx. This gives rise to paroxysmal attacks of coughing, which are extremely painful by reason of the ulcerated condition of the structures forming the upper part of the laryngeal opening. In such case no rest can be obtained, and the exhaustion and general prostration are extreme.

Towards the end of the second week a morbilliform eruption of septic origin may appear on the buttocks, cheeks, and extensor aspect of the larger joints; and the case may rapidly prove fatal. Death may not occur until the third week, in which case suppuration is very prone to arise in connection with some of the lymphatic glands, or elsewhere. Further symptoms, which usually set in before death and afford evidence of the septicæmic nature of the case, are profuse diarrhœa, restlessness, delirium, sweating, pulmonary congestion, broncho-pneumonia, wasting and albuminuria. In cases which recover, the pyrexia and other symptoms usually show a gradual abatement during the latter half of the second week; but even in these the duration of the acute illness is seldom less than a fortnight. Wasting is considerable, and convalescence, often interrupted by the advent of some well-recognised complication, is correspondingly protracted.

3. *Toxic Scarlet Fever.*—This form of attack includes those cases which are often described by the terms Scarlatina Maligna, Ataxic or Adynamic Scarlet Fever. The characteristic feature is that the gravity of the patient's condition is out of all proportion to the severity of the throat lesion. In the true malignant attack the patient is struck down by the intensity of the scarlatina poison, and dies even before the typical symptoms of the disease have had sufficient time to show themselves. The rash, if present at all, is patchy and ill-developed; there is but little affection of the fauces, the pulse is extremely rapid and feeble, and the patient, often conscious to the end, succumbs with the signs of

profound nervous depression, and a temperature which, as in snake-bite, may have been subnormal throughout.

Such cases at the present day, in London at any rate, are extremely rare; whatever may have been the case in the past. Not infrequently, however, a type of attack is met with which by its toxic intensity is deserving of the name "Semi-malignant." It presents the following characters: the signs of invasion are usually inordinate, especially the vomiting, which often persists throughout; the temperature soon rises to a great height, perhaps to 106°, and is for the most part sustained, with but slight remission; the rash quickly appears, and becomes intensely vivid, with a tendency to cyanosis, best marked in the lips and extremities; petechiæ sometimes appear in the skin, which may become much discoloured in dependent parts; the fauces are vividly injected, and more or less œdematous, but there may be no ulceration whatever, or any obvious infiltration of the subjacent lymphatics; the pulse is very frequent, often, in children, reaching 180 by the end of the second day. Vomiting, intense restlessness, muscular tremor, and mental confusion are always present, the latter passing through the stage of delirium into final coma. Death commonly takes place on the fifth or sixth day. Towards the end of these cases the temperature often shows a further elevation. It may register above 106° at the time of death. Cadaveric lividity always sets in rapidly, and signs of its approach are often noticeable before life is extinct. As in typhus fever, this condition simply represents the final development of a petechial eruption coupled during life with some degree of cyanosis, and may be regarded as an expression of the intense toxic disintegration which has taken place in the blood.

It should be remarked that the term "malignant" is often loosely applied to that class of case which is here described under the name "septic." True it is that many of such cases, from one point of view, are malignant—indeed very malignant; but in them the dominant symptoms are dependent upon the relative severity of a local lesion which may be regarded as more or less contingent to scarlet fever. It seems to me more logical to restrict the term "malignant" to those cases which are malignant in virtue of the intense action of the essential scarlatinal poison.

VIII. Analysis of Symptoms.—*Aspect.*—The facial expression in scarlet fever, at any rate at an early stage of the attack, is usually intelligent. The eyes are bright and sparkling, and the conjunctivæ during the first two days are commonly somewhat injected, especially if the rash be well developed. The cheeks are from the first suffused with a vivid flush, which, on the second or third day of the eruption, becomes as it were dusted over with a fine white powder, giving rise to an appearance of powder and rouge which is very suggestive of the stage. This is in reality the earliest sign of peeling. In many cases the powdering is so fine that it might not inaptly be compared to the bloom on a ripe peach, and tends greatly to enhance the natural beauty of childhood. Its characters may be clearly defined by the aid of a magnifying lens. The forehead, too, is not infrequently flushed, but to a much less extent. The region around the mouth is never invaded by a flush or rash of any description, but stands out pale and white in marked contrast to the vividly injected cheek. This circumoral pallor forms a well-defined circle or triangle, bounded laterally by the naso-labial folds, and below by the point of the chin. It is well brought out in a photograph, and though by no means distinctive of scarlet fever, is of considerable diagnostic value as a point of differentiation from measles.

After the fall of the temperature, and the decline of the rash, the complexion loses these characteristics, and the countenance generally becomes somewhat pallid. The pallor is partly the result of powdery desquamation, and is in some degree dependent upon a condition of post-scarlatinal anæmia. In very mild attacks, with slight eruption, there may be very little of the foregoing appearances.

Eruption.—The scarlatinal rash is very characteristic, appearing usually within twenty-four hours after the symptoms of definite invasion; it is first seen on the chest, neck, and upper arms, from thence it spreads, in the course of a few hours, over the trunk, down the arms, and finally reaches the legs, extending from above downwards. In well-marked cases it usually reaches its height in three days, that is on the fourth day of attack. Its full development on the lower part of the legs may be as much as twenty-four hours later than on the chest and neck. Its colour may be best described as a bright brick red, varying in mild attacks towards pink, and showing a tendency to the darker scarlet tints in severe cases. Intensity and persistence usually go together, with a proportionate tendency to staining.

There are two elements in the developed scarlatinal eruption—a finely papular or so-called punctate element, which is usually the first to appear, and always the last to go; and a superadded erythema, representing the confluent element. This is more transient, and disappears earlier than the fine papulation referred to. It will be obvious, therefore, that the rash in its earlier stage is mainly papular; in its developed stage it is both papular and erythematous, and in its final stage it is again papular. In many cases, however, the rash is of a mixed character from the outset. By careful attention to the relative development of these two factors on different parts of the surface, it is usually possible to gauge with some degree of accuracy the stage at which the attack is presented. Confirmatory evidence of great value can also be deduced from the appearance of the tongue at the same stage. The rash when fully developed is attended with a considerable amount of inflammatory œdema, causing more or less difficulty in flexing the finger-joints.

The eruption fades in the order in which it appeared, going hand in hand with the rise and fall of the temperature. In well-developed cases the rash is gone by the end of the week, leaving behind a uniform greenish yellow discoloration of the skin. This is best recognised by pressing with the finger on the surface of the abdomen, and then rapidly withdrawing it. In some instances distinct lines of hæmorrhage may be discerned for several days running transversely across the flexor surface of the elbows, wrists, and knees.

Certain local peculiarities of the eruption are deserving of notice. In the first place, it may be emphatically stated that a true scarlatinal eruption is very rarely seen on the face; what is seen is, as has been stated, simply an erythematous flush, best marked on the cheeks, and often in less degree on the forehead. No punctation, still less papulation, is to be found in the vast majority of cases. The same distinction is true of the palms, and still more of the soles.

Although the distribution of the minute papulation may be to some extent determined by the points of emergence of hairs, yet this is by no means the rule; for the large majority of these tiny papules do not correspond in locality with the hair follicles, or, if so, only by accident. However, the local anatomical peculiarities of the skin are not altogether without effect on the development of the scarlatinal eruption. Where the skin surface is coarsely papular, as for instance on the outer surface of the upper arms and on the outside of the legs and thighs, it will be found that the rash is characterised by numerous coarse and indurated papules. These, however, may be normally present, in which case they are simply rendered more obvious by the hyperæmia which is an essential feature of the scarlatinal eruption. But although in their nature these papules may not be strictly scarlatinal, they nevertheless afford valuable indications of a recent eruption, as, by retaining their injection, they may remain unduly obvious for at least a week after the true rash has disappeared. The diagnostic value of this coarse papulation on the outer side of the legs and upper arms during the second week of scarlet fever can hardly be overestimated.

During the decline of the eruption the tension in the skin gradually relaxes as the œdema disappears, and a somewhat shrivelled, parchment-like appearance and feel of the epidermis affords a trustworthy indication of the peeling which is to follow.

In some cases, in consequence of the intensity of the rash, the minute papules which characterise the scarlatinal eruption actually proceed to vesiculation, and so give rise to localised crops of miliaria. They differ in their appearance from those seen in acute rheumatism in the fact that each one is situated upon an obviously inflamed base. They most often occur upon the back of the hands, wrists, and forearms, more rarely on the neck, chest, and abdomen, and often give rise to considerable irritation.

Desquamation.—A certain amount of peeling of the cuticle will be found in all cases which have been attended with a distinct eruption. Whether peeling ever occurs in cases in which there has been absolutely no rash, is however less certain. Its amount is usually proportionate to the intensity and persistence of the eruption. Desquamation bears the same relation to the antecedent eruption as peeling of the tongue does to the previous inflammatory injection of the mucous lining of the mouth and fauces. In infants, in whom the skin is soft and fatty, the subsequent peeling is usually but slight and transient, and, unless looked for with the greatest care, may escape observation altogether. It may be best observed by rubbing the skin with a towel after the child has been bathed, when delicate rolls of cuticle will generally be seen to come off for several days after the rash has faded. Peeling, too, is often slight and ill-defined in adults who have passed through a mild attack. The only sign of its presence in persons in whom the skin is naturally greasy, as it often is in young adults who are the subjects of acne, may be a late separation in shreds of the thick epidermal covering of the palms and soles.

The local peculiarities of the skin in different parts of the body exert a modifying effect upon the character of the desquamation. Thus, on the face and ears it usually takes the form of a fine powdering, and the same may be true of the groins, axillæ, and inner side of the upper arms. On the neck, trunk, forearms, and thighs the surface epidermis separates in the form of delicate scales of variable size, commonly preceded by a pin-hole or worm-eaten appearance of the cuticle which is very distinctive. From these numerous centres the peeling extends centrifugally, until, by fusion of their peripheries, any such arrangement is imperceptible. The skin covering the front of the knees usually desquamates in coarser scales and in less characteristic fashion. This is still better marked as regards the palms and the soles, from which the cuticle usually comes off in shreds or large thick flakes. In some instances these are so extensive as to resemble an incomplete glove or golosh; whereas in others, a dry and chalky appearance of the palms and soles is all that can be found to represent desquamation. It has been said that the nails are occasionally shed as a part of the general desquamative process, but I have never seen this occur.

The earliest sign of desquamation will be found on the face in the form of the fine powdering on the cheeks, which, if the subjacent flush be well marked, gives rise to the powder and rouge appearance before referred to. In many cases the powdering is of a coarser character, and may be earliest and best marked on the frontal eminences, the eyelids, the muco-cutaneous junction of the lips, the lobules of the ears, and at the margin of any scab or recent cicatrix wherever situated. In well-developed attacks the peeling may be visible on the face as early as the second day of the rash. It rapidly extends, and by the end of the week is well marked on the neck, chest, and inner surface of the arms. By the end of the second week peeling will have become more or less general. The face and neck by this time will usually have completed their peeling, and evidence of that which is to follow may either then, or a little later, be observed on the palms and soles, which feel dry and parchment-like, and present a somewhat wrinkled appearance. At the end of four weeks peeling in most cases will have been completed, with the exception of the palms and soles, which do not become clear as a rule until two or three weeks more have elapsed.

withdrawing it. In some instances distinct lines of hæmorrhage may be discerned for several days running transversely across the flexor surface of the elbows, wrists, and knees.

Certain local peculiarities of the eruption are deserving of notice. In the first place, it may be emphatically stated that a true scarlatinal eruption is very rarely seen on the face; what is seen is, as has been stated, simply an erythematous flush, best marked on the cheeks, and often in less degree on the forehead. No punctation, still less papulation, is to be found in the vast majority of cases. The same distinction is true of the palms, and still more of the soles.

Although the distribution of the minute papulation may be to some extent determined by the points of emergence of hairs, yet this is by no means the rule; for the large majority of these tiny papules do not correspond in locality with the hair follicles, or, if so, only by accident. However, the local anatomical peculiarities of the skin are not altogether without effect on the development of the scarlatinal eruption. Where the skin surface is coarsely papular, as for instance on the outer surface of the upper arms and on the outside of the legs and thighs, it will be found that the rash is characterised by numerous coarse and indurated papules. These, however, may be normally present, in which case they are simply rendered more obvious by the hyperæmia which is an essential feature of the scarlatinal eruption. But although in their nature these papules may not be strictly scarlatinal, they nevertheless afford valuable indications of a recent eruption, as, by retaining their injection, they may remain unduly obvious for at least a week after the true rash has disappeared. The diagnostic value of this coarse papulation on the outer side of the legs and upper arms during the second week of scarlet fever can hardly be overestimated.

During the decline of the eruption the tension in the skin gradually relaxes as the œdema disappears, and a somewhat shrivelled, parchment-like appearance and feel of the epidermis affords a trustworthy indication of the peeling which is to follow.

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In some persons the period of desquamation extends to the length of three or even four months, but the majority will have finished their peeling in from six to eight weeks. Redesquamation not infrequently occurs, but is rarely more than partial.

A slight furrow running transversely across the nail often serves as an indication of a previous scarlatinal eruption. These depressed lines, which not infrequently have a dotted appearance, may be seen above the bed of the nail during the course of the third week, and, rising as the nail grows, they usually reach the free border in four or five months. Though met with in other fevers, they but rarely reach the same degree as in many cases of scarlet fever.

Temperature.—Rising rapidly with the first symptoms of invasion, the temperature usually reaches its climax on the third or fourth day of the disease, by which time the rash also will have attained its full development. After this the course of the temperature will vary with the type of attack. In simple scarlet fever it proceeds *pari passu* with the eruption, showing a gradual decline until the normal is reached by about the end of the week, or, in very mild cases, a day or two sooner. During the first three or four days the diurnal variation is but slight, the evening temperature being usually a degree or two higher than the morning record. Throughout the lysis, which coincides with the latter half of the week, the daily excursion is commonly somewhat wider, showing perhaps a difference of more than two degrees between the morning and evening records. In this form of attack the temperature but rarely reaches 105°, even in the evening of the third or fourth day. It usually varies at this stage between 102° and 104°, and its subsequent decline is commonly more gradual than its previous ascent.

In the septic form of attack the temperature, instead of showing a gradual fall to normal during the latter half of the first week, continues at about the same level; but the daily variations become wider as the septic features of the illness become more pronounced. Subsequently the course of the temperature will naturally depend upon the ultimate character of the disease. In favourable cases a gradual return to normal usually commences at some time during the course of the second week, and defervescence, even if uninterrupted by any definite complication, may take another week before it is complete. In the toxic variety the temperature is maintained at a higher level, and is less remittent. It usually averages about 104°. Most of these cases, however, die without any abatement of pyrexia before the end of the first week. Indeed, the temperature may register 106° or more at the time of death.

It may be definitely stated that anything approaching a true temperature crisis in scarlet fever is an event of the greatest rarity. I have not met with as many as half-a-dozen amongst some 12,000 cases of the disease.

Pulse and Respiration.—The only feature of the scarlatinal pulse which is deserving of mention is an undue rapidity, usually seen during the first thirty-six or forty-eight hours of the attack.

This is best marked in those toxic cases which are attended with persistent vomiting and hyperpyrexia; but even in simple scarlet fever, the pulse of a child of five years old may register 160 per minute at the commencement, although the temperature may be not higher than 103°. After the second day this character is usually lost. The arterial tension is high, and the vessel more often feels small than the reverse. During convalescence an unusually slow pulse is occasionally observed in adults.

The frequency of the respiration seems to vary more with the height of the temperature than the rapidity of the pulse, and the expired air is highly charged with carbonic acid.

Fauces.—The typical scarlatinal throat is represented by a vivid red injection of the mucous membrane of the fauces, palate, and uvula, attended with some degree of inflammatory œdema, and more or less swelling of the tonsils. The degree to which the tonsillar swelling may attain is dependent upon the severity of a parenchymatous tonsillitis associated with the scarlatinal process; and its amount may be regarded, in a sense, as more or less of an accident. There is really nothing in its appearance to distinguish a scarlatinal throat, in mild cases, from a simple tonsillitis or faucial catarrh. The mucous membrane often presents an angry red appearance with a tendency to become dry and sticky.

In certain cases, especially those in which the inflammation is very acute, the surface of the tonsils may be coated with a pellicular formation, occurring either in patches or in a continuous layer. In rare instances the exudation may extend beyond the limits of the tonsils, and even encroach on the palate or side of the uvula. This must not be taken as evidence of coexistent diphtheria. In some cases it is obviously a thin exudation lying upon the surface of the tonsils; in which case it soon separates or becomes disintegrated, giving rise to a very superficial ulceration which rapidly heals. In others, instead of being raised above the surface, it is somewhat depressed, and represents a surface necrosis of the tonsil, which separates later as a distinct slough.

In the septic form of attack the characteristic ulceration of the tonsils may originate in like manner; on the other hand, the process may begin as an ulcer, which, by its extension in all directions, leads to such widespread destruction of tissue that the mechanism of the parts is greatly interfered with. At a late stage of such an attack, any attempt to swallow results in regurgitation of fluid through the nostrils, and the entrance of food and offensive secretions into the laryngeal orifice. This not only leads to constant distress, but undoubtedly tends to rapid development of septic bronchitis and broncho-pneumonia.

The offensive muco-purulent rhinorrhœa so constantly present in septic attacks is dependent upon ulceration affecting the naso-pharynx, whence, in consequence of the swollen and painful condition of the tonsils, the discharge finds a more ready escape through the anterior nares.

Tongue.—Of all the symptoms in scarlet fever the tongue presents perhaps the most characteristic. As in simple tonsillitis, the tongue rapidly becomes coated with a thick, white, creamy fur in consequence of an active proliferation of its normal epithelium. It then cleans with almost equal rapidity, and in well-developed attacks may become completely denuded of its epithelial covering by the end of the third day. Peeling of the tongue begins at the tip and edges, which, as early as twenty-four hours from the appearance of the eruption, may show up red and raw-looking in marked contrast to the thickly-furred dorsum. Occasionally, even at this stage, the red tips of the fungiform papillæ may be observed peeping out through the fur which thickly covers the dorsum, and thus give rise to an appearance very similar to that of an unripe strawberry. Rapid separation of the epithelium then occurs, frequently in patches. The process of denudation, which commences at the tip and edges, extends centripetally; and by the third or fourth day the tongue is completely stripped of its epithelium, the region of the circumvallate papillæ being the last to clear. The tongue at this stage greatly resembles a ripe, red, and succulent strawberry. It may not inaptly be compared to the appearance of a piece of raw beef, especially if the surface become somewhat dry and glazed, which it frequently does at a little later stage. Its strawberry-like appearance is greatly enhanced by the relative prominence of the fungiform papillæ. It must be remembered that the completeness with which the tongue peels is proportionate to the degree of inflammatory injection of the faucial and buccal mucous membrane. In cases which are characterised by very mild throat symptoms one does not expect to find so typical a development of the strawberry tongue. The value of the tongue as a diagnostic sign will be obvious when it is stated that no other form of sore throat whatever, but that due to scarlet fever, is attended with a clean, much less with a raw-looking tongue. Towards the end of the week the epithelium again begins to be restored, and consequently the tongue at this stage usually presents a delicate silvery appearance.

In septic attacks the tongue during the second week again becomes coated, but not with the white, creamy fur so characteristic of the earlier stage. In severe attacks the organ not infrequently becomes affected with an aphthous-looking ulceration, which may also involve the gums and buccal surfaces of the cheeks and the lips; in this case it is not uncommon for the angles of the mouth to become sore and fissured.

In occasional instances the peeling of the tongue remains limited to the tip, the edges, and a longitudinal strip down the centre which often presents a somewhat ragged appearance. Gresswell, under the names "triareal" and "pentareal," has described certain peculiarities of the tongue which he has met with in some cases. They are certainly exceptional, and, moreover, their relation with scarlet fever is at least doubtful.

Glands.—Some degree of enlargement of the glands lying beneath the ramus of the lower jaw probably occurs in all cases of scarlet fever which are attended with definite faucial inflammation. In most cases a distinct fulness may be observed, accompanied by more or less tenderness on pressure. The pain experienced on swallowing is mainly dependent upon the pressure which is exerted upon these glands by the muscles during the act of deglutition.

In septic cases the glandular enlargement is considerable, and the tenderness may be acute. Suppuration, moreover, is not infrequent. In very severe cases the adenitis is often associated with a low form of periadenitis, and the infiltration of the cellular tissue may increase to such an extent that the neck becomes encircled by a collar of inflamed tissue, giving rise to the appearance known as "bull-neck." The swelling becomes red and brawny, and small foci of suppuration usually occur in its substance. If it be incised, the feeling to the knife is like that of cutting through hard bacon rind; and a thin, blood-stained serum exudes which has strongly irritant properties. Occasionally portions of the skin break down, and sloughing of the subjacent cellular tissue may occur to such an extent that the deeper structures of the neck become exposed to view. Such patients usually die about the end of the second week, or a few days later; and a fatal hæmorrhage may occur in consequence of the wall of a vein becoming involved in the sphacelus. Hæmorrhage resulting from the perforation of an artery is excessively rare. An abscess not infrequently forms in one or more of the glands lying deep under the sterno-mastoid; in this case the suppuration is attended with considerable local swelling, and an aggravation of the constitutional symptoms.

Nervous System.—In simple scarlet fever a variable amount of mental obscuration with a tendency to wander at night time is not uncommon. These signs are usually associated with a high temperature, and commonly appear on the third or fourth day when the fever is at its height. It should be remarked, however, that the headache, pains, and vomiting which mark the early stage are also evidences of an affection of the nervous centres. In severe attacks the involvement of the nervous system is much more pronounced. In young children the attack may be ushered in with a convulsion; but though severe chills are commonly complained of, a distinct rigor in scarlet fever is decidedly rare. If the temperature be much elevated, delirium may appear as early as the second night of the attack, with a tendency to become continuous during the latter half of the week; in adults under these circumstances it may be of a violent character and necessitate some form of restraint.

During the course of the second week, as the strength fails, the delirium tends to become more of the muttering type. Muscular tremor, picking at the bed-clothes, and loss of control over the evacuations, appear in bad cases. Towards the end the signs of cerebral exhaustion gradually merge into fatal coma, death being not infrequently attended or preceded by a rise of temperature which probably results from excessive disturbance of the heat centres. Delirium in young children is apt to be overlooked, as they are less accustomed to give expression to ideas. In them a blunted receptive faculty, coupled with restlessness and a tendency to purposeless movements, may be the only signs of mental impairment.

In cases of the toxic variety the initial signs are usually very severe, and the vomiting may persist throughout. Muscular tremor is rarely absent, but in some cases a tendency to tonic spasm is indicated by some retraction of the head and the presence of more or less trismus. In others, an attack of general convulsions supervenes at a late stage, which usually terminates fatally. Though dull and confused in mind, if not actually delirious, the patient is intensely restless, and resents interference of any kind. The excreta are passed involuntarily, and the mental stupor soon passes into final coma. This form of attack, which in many points is very suggestive of typhus, is sometimes known by the name of "Ataxic scarlatina" in consequence of the profound affection of the nerve centres. Temperatures of 112° and 115° have been recorded in exceptional instances; they are almost invariably fatal, and such a case is difficult to manage, as the patient resents both feeding and treatment.

Excretions.—1. *Urine.*—The urine during the pyrexial stage presents the characters which are usually associated with the febrile condition. It is scanty, high-coloured, unduly acid, and contains, in proportion to its bulk, an excess of the normal solids. The chlorides, however, are diminished, if not entirely absent. During the first few days the amount of urea passed will be found to vary directly with the degree of pyrexia, a temperature of 103° being sometimes associated with the passage of urine containing as much as 4 per cent of urea. About the time, however, when the rash has reached its full development, usually the third or fourth day, this relation between the height of the temperature and the amount of urea commonly disappears. The urea then frequently shows a sudden drop to even less than 2 per cent, although the temperature may remain at the same height. In some cases, after the lapse of a few days, the amount of urea will again show a temporary rise, although the temperature may have progressively decreased. During the height of the fever, the urine, as in other febrile disorders, not infrequently contains a trace of albumin, which quickly disappears as the temperature falls.

The sudden appearance of urine rendered smoky by the presence of blood is due to definite nephritis. Such, too, is the case if the urine be found to contain a progressively increasing quantity of albumin, even though unattended with hæmaturia. In such cases it is usually passed in somewhat diminished quantity at first, and contains a lessened amount of urea. At a later stage, however, more or less diuresis supervenes, and the daily loss of albumin is increased, although the total amount of urea excreted may still remain below the normal. The faint and transient clouds of albumin which frequently occur during the convalescent stage of scarlet fever have been the subject of considerable difference of opinion. These evanescent traces are certainly very common, occurring possibly in as many as 30 or 40 per cent of cases. Whatever view may be taken of their pathology, they are apparently devoid of any prognostic significance.

With the onset of convalescence the urine gradually loses its febrile characters, and is excreted in greater quantity. It is pale and limpid when passed, but a nebulous deposit composed of mucus and phosphates usually forms at the bottom of the vessel on standing.

The daily output of urea rapidly diminishes, attended with a corresponding fall in the specific gravity. The chlorides reappear at an early date, usually before the temperature has fallen to normal.

A toxine has been extracted from scarlatinal urine which, like the leucomaine found in the urine of enteric fever, can only be regarded as a derivative.

I have never been able to detect the so-called prealbuminuric hæmoglobinuria recorded by the late Dr. Mahomet, nor does its occurrence seem to have been noted by any subsequent observer. A slight degree of peptonuria is not very uncommon in scarlet fever, a fact which should be remembered when testing for the presence of albumin; moreover, the urine frequently contains a trace of mucin.

2. *Bowels.*—The bowels are usually confined during the febrile stage, and may remain so as long as the patient is confined to bed; but diarrhœa is frequently an early symptom in sharp attacks. Diarrhœa, too, often appears towards the close of a septic case, and the stools then become exceeding offensive.

3. *Skin.*—In most cases which have been attended with a well-developed eruption the skin remains dry throughout, but in a certain proportion an imperfect diaphoresis occurs, leading to the formation of copious miliaria. Excessive perspiration often comes on after peeling is completed. It is best marked on the hands and feet, which frequently become bathed in sweat, both during sleep and under the stimulus of the slightest mental excitement. This tendency in adults may last for several weeks after desquamation is completed.

IX. Aberrant Cases.—There is considerable difficulty in the diagnosis of many cases of scarlet fever by reason of an *unusual mildness* of the attack. The symptoms may be there, but yet so ill-defined and transient as readily to escape observation. For their recognition an intimate acquaintance with the phenomena of the disease is essential, and also the opportunity of observing them at the right moment. Such attacks are most common in infants, and in adults who at some time previously have suffered from scarlet fever. Family idiosyncrasy, too, in respect to mildness of attack, is as well established as it is in the direction of severity. In some undoubted attacks the whole duration of the febrile stage may not extend over three days, occasionally it is even less. Though capable of imparting the contagion, the patient is probably infectious to a much less extent than if the subject of a well-developed attack.

Excessive mildness is characteristic of those cases known as "Surgical Scarlet Fever," which so often arise in the wards of an hospital. That the type of attack should be so uniformly mild, is very possibly due to the fact that the patient, in virtue of a previous operation, wound, burn, or other breach of surface, or even that unknown conjunction of ward influences known as "Hospitalism," is thereby rendered so susceptible that he reacts to a minimum dose of the contagion — a dose which, either by reason of its excessive smallness or its feeble virulence, might be quite inoperative in normal health; and even in the patients lowered to some extent by these influences, seems not to possess sufficient power to prevail against the vital resistance of the blood and tissues. The term "Surgical Scarlet Fever" is somewhat misleading; the same mildness is frequently found to characterise the disease when it arises in the subjects of various medical ailments.

Again, certain cases of scarlet fever are aberrant by reason of the more or less complete *absence of one or other of the symptoms of the disease.* Thus the form of attack which sometimes affects nurses and others in frequent contact with the disease may be cited in point. Such attacks are known by the name of "Abortive Scarlet Fever," or "Scarlatina sine eruptione." As their name implies, they are marked by an absence of any eruption—sore throat, attended with fever of short duration and slight degree, being the only obvious symptoms. In other cases the eruption may be visible, but the faucial affection practically absent, and the tongue show no sign of peeling whatever. This form of attack is most common in adults, in whom, too, the early rapidity of pulse is frequently wanting. In cases of the foregoing kind the later appearance of one of the recognised complications (see p. 150) may assist in confirming a diagnosis otherwise doubtful.

An attack of scarlet fever may be aberrant by reason of its distinctive characters *being masked by the presence of another exanthem* [see "Coexistence of Infectious Diseases"]. Thus the eruption of scarlet fever may be blended with that of chicken-pox or measles, and in several instances I have seen the rashes of all three mingled in the same individual. Although the large majority of faucial exudations met with during the acute stage of scarlet fever are not diphtheritic, it is well to remember that the two diseases are occasionally coexistent; in such a case the special features of diphtheria are superadded to those of scarlet fever, and the combination is usually very dangerous.

When scarlet fever arises in a person who is at the time suffering from eczema or psoriasis, the appearance of the eruption may be very misleading. Irregular red patches of inflamed skin are presented on various parts of the body, which occasionally bear some resemblance to the rash of measles; but the raised patches are usually harsh and scaly, instead of yielding the soft velvety feel so characteristic of this disease. The subsequent peeling is excessive, and appears very early in the attack. Scarlet fever, arising in a strumous child who is suffering from conjunctivitis, may, at an early stage, be very suggestive of the onset of measles, especially if the rash present the morbilliform conformation seen in certain rare cases which are characteristic in other respects.

Puerperal scarlet fever, that is scarlet fever arising immediately before or after confinement, is a conjunction which my experience leads me to view with the greatest anxiety, although it must be admitted that some physicians of experience regard it without apprehension. It would seem that the danger to life enormously increases with the proximity to the time of delivery at which the symptoms of the disease appear. In my own practice three cases died out of four, in which the rash appeared within four days of parturition; and it should be remembered that the onset of labour may be one of the invasion symptoms of the disease itself. This, however, but rarely occurs unless the woman has almost completed her full term. In puerperal scarlatina it is not that the strictly scarlatinal symptoms show an undue severity, but during the few days following delivery, in spite of the most rigid antiseptic precautions, there is a great tendency to the gradual development of puerperal septicæmia. The rash in such cases is usually very intense, and the temperature remains persistently high. The sapræmic condition may lead to the development of coma, and the gradual failure of the heart's action without the intervention of peritonitis or other localised inflammation of a septic character. Such, at any rate, has been my experience in cases of undoubted scarlet fever arising during the early puerperal state.

X. Differential Diagnosis.—If attention be paid to the symptoms already described, a well-developed case of scarlet fever can hardly be mistaken for any other disease. In mild and ill-defined attacks, however, considerable difficulty may be presented by reason of their negative aspect. The diseases with which scarlet fever may most readily be confounded are tonsillitis, diphtheria, measles, rötheln, and early smallpox; besides various other affections which may give rise to difficulty in exceptional instances. Influenza, simple febrile catarrh, erysipelas, erythema, desquamative eczema, and even the rashes of belladonna and copaiba, have all of them been mistaken for scarlet fever.

From tonsillitis the diagnosis may be very difficult—in some instances quite impossible. It should be remembered that in tonsillitis there is usually an absence of vomiting, the skin appearance, if present, is represented by a simple erythema, limited usually to the chest and neck, and there is no papulation or even punctation. The swelling of the tonsils is often, for a time at least, more obvious on one side than the other; and, if other distinctive signs of scarlet fever be wanting, a high temperature may be taken as evidence in favour of tonsillitis. The tongue remains coated throughout, having a pasty appearance; and it shows no sign of peeling even at the tip and edges. The attack, moreover, is not followed by desquamation.

Scarlet fever attended with faucial exudation may be mistaken for true diphtheria, especially as a redness of the skin is occasionally seen in the latter disease. Here, however, as in tonsillitis, it is simply a flush devoid of any punctation. It is usually limited to the chest and neck, and is very transient. (For other points of distinction, see "Coexistence of Infectious Diseases.")

From rötheln the diagnosis may be by no means easy. In this disease reliance should be placed upon the slightness of the pyrexia, and the absence of vomiting, headache, or any peeling of the tongue. The faucial affection is very slight, mild catarrh is frequently present, and also a tenderness, often complained of by the patient himself, of the concatenate glands, especially those lying over the mastoid and occipital bones. Some enlargement of these glands is common in scarlet fever, but usually to a less extent. The rash for a time may be suggestive of scarlet fever, but sooner or later it usually conforms more to the measles type, though commonly more discrete and pinker; moreover, it is frequently seen upon the face and forehead, and even the circumoral region may be invaded. Slight desquamation of the trunk and limbs may follow, but the peeling never shows the pinhole conformation.

At an early stage scarlet fever may be confounded with measles, especially if there be much conjunctival injection, and the rash be at all blotchy, or show a tendency to aggregation of its papular constituents. In this case irregular tracts of raised and inflamed skin may be presented. In measles a definite history of two or three days' previous illness, with cough, sneezing, and lachrymation, can usually be obtained; but vomiting is usually absent. The course of the temperature varies in the two diseases; that of measles usually falls suddenly within forty-eight hours of the appearance of the eruption, instead of declining gradually with it. The catarrhal symptoms are a prominent feature throughout the attack of measles, whereas the throat affection is limited to an inflammatory redness of the faucial and buccal mucous membrane. Although the tongue often cleans rapidly, its peeling is rarely so complete as to give it a strawberry appearance; moreover, the rash usually affects the face, and has a marked tendency to invade the forehead and circumoral region; measles spots, too, are commonly seen at an early date behind the ears, and at the margin of the hairy scalp. Towards the end of the second week of a septic attack of scarlet fever an eruption of raised spots or somewhat larger blotches may appear, and give rise to the suspicion of an intercurrent attack of measles. Their distribution is usually limited to the cheeks, buttocks, extensor surface of the larger joints, and parts which are subjected to pressure. The points of distinction from measles are that the spots are usually more raised; they are either of a brighter tint, or of a more distinctly brown colour, and they are usually less persistent than is the rule in that disease. They frequently fade only to reappear in the course of a few hours, and can always be made to disappear on pressure. This septic eruption, which is also met with in some bad cases of diphtheria, is unattended with the catarrhal signs so characteristic of measles.

The initial rash of an erythematous and sometimes punctate character which is found in certain cases of small-pox may be mistaken for scarlet fever during the first few days, although the eruption is usually confined to the lower part of the abdomen, groins, and axillæ. Vomiting is a common initial symptom in both diseases, but a definite rigor, though common in small-pox, is rarely seen in scarlet fever. Severe pain in the back, too, is very suggestive of the former disease, but the appearance of the small-pox eruption on the third day, and the absence of peeling of the tongue, will settle any previous doubt.

The diagnosis of scarlet fever in the post-febrile stage will mainly depend upon the presence of characteristic desquamation, and the advent of some one or more of the recognised complications of the disease (see p. 150). It should be remembered that the tongue may retain more or less of the strawberry character for about a week after it has fully peeled; although the central portion may again become slightly coated towards the end of this period. The coarse papulation on the outer side of the legs may remain visible for at least a week after all other signs of the eruption have disappeared, and slight staining may be observed on the trunk for several days after a well-developed eruption has faded. A fulness or palpable enlargement of the glands beneath the jaw may remain for several days as evidence of a previous faucial inflammation. The diagnosis may be strengthened by ascertaining the mode of invasion, and whether the patient has or has not been recently exposed to the infection of scarlet fever. Inquiry also should be made as to the nature of any outbreak which may have been prevalent in the locality.

XI. Prognosis.—In addition to any general consideration, such for instance as the epidemic type, or the slight possible influence which has rightly or wrongly been ascribed to season, the case mortality is to a large extent dependent upon certain personal factors, of which the following are perhaps the most important :—

Age.—The fatality of scarlet fever is greatest in early childhood; it shows a progressive diminution from the first year of life until about the age of puberty, whence, until the twenty-fifth year, it remains at its lowest. After this age the death-rate shows a slight and somewhat regular increase in relation to advancing years. By referring to Table III. it will be seen that the case mortality during the first quinquennium is more than three times as high as in the second, and seven times as high as in the third. The slight rise which marks the fatality of scarlet fever after the twenty-fifth year at no time in life again quite approaches the mean.

Sex.—The influence of sex is not very great. The combined mortality in males at all ages is greater than it is in females by 1 per cent—the death-rate of the two sexes amongst the cases enumerated in Table III. being 8·8 and 7·8 respectively. From this table it also appears that although the aggregate mortality during the first quinquennium proved to be greater in males than in females by more than 1 per cent, yet amongst 13,833 cases of this age period admitted during the years 1888-1893, the mortality was greater in females during the first three years of life than it was in males.

State of Health.—The unfavourable influence of the strumous or tubercular diathesis is well seen in the tendency which is often noticed in cases of pulmonary phthisis for a fatal issue to be hastened by an attack of scarlet fever, although the disease may have been previously latent, or at most have been pursuing a chronic course. So, too, a condition of ill nutrition, associated with poverty and a defective hygiene, undoubtedly disposes to a severe attack. This is shown by the greater fatality which is found in scarlet fever amongst the inhabitants of the poorer districts of London, even though removed to hospital at an early date.

The tendency of puerperal women to fatal septicæmia as a direct consequence of the scarlatinal attack has been already referred to (see Aberrant Cases). The subjects of previous renal disease are almost invariably affected with a recrudescence of inflammatory changes in the kidneys, which often leads to uræmia and a fatal termination.

Although the attacks of so-called "Surgical Scarlet Fever"—that is, scarlet fever occurring in the subjects of recent wounds or operations, or in those who are at the time affected with some disease which has confined them to bed—are usually characterised by excessive mildness, nevertheless it is not uncommon for those who are actually suffering at the time from some other infectious disorder to have the disease in a severe form. If the attack supervene during convalescence it is frequently of a benign character, and might deservedly be ranked amongst the so-called "surgical cases." [See "Coexistence of Infectious Diseases."]

In addition to the increase of the gravity of a case of scarlet fever by the advent of any of the recognised complications, there are certain symptoms of the primary attack which are of unfavourable omen. Ulceration of the fauces, attended with gland infiltration, rhinorrhœa, high temperature, and perhaps the appearance of a later septic eruption, are indications of the septic form which the disease is assuming. In the same way hyperpyrexia, extreme restlessness, and a vivid rash, accompanied by a rapid, feeble pulse, early obscuration of mind, tremor, and persistent vomiting, are evidences of a toxic attack, and of consequent danger to life. Delirium in scarlet fever always indicates a severe attack, especially when it occurs in adults. About 80 per cent of cases showing a septic eruption are fatal, and a petechial eruption, with cold and cyanotic extremities, is an exceedingly unfavourable sign.

XII. Complications.—Although the large proportion of deaths attributable to scarlet fever are due rather to the severity of the attack in its acute stage than to any of its later developments, the complications of the disease are of considerable importance in view of the tendency of some of them to become chronic, and, if neglected, to lead to permanent impairment of health.

Of the recognised complications the following table enumerates the most important. Those occurring in less than 1 per cent of cases are omitted from the table, but will be referred to later.

TABLE IV.—Showing percentage incidence of Complications amongst 4015 cases of Scarlet Fever treated in the South-Western Fever Hospital, Stockwell, during the years 1890-1892.

Otitis (with discharge)	occurred in	11·05	per cent.
Adenitis (cervical)	,,	8·74	,,
Rheumatism (articular)	,,	4·50	,,

Albuminuria (simple)	occurred in	4·23	per cent.
Nephritis (acute)	,,	3·41	,,
Eczema	,,	2·11	,,
Ulcerative stomatitis	,,	1·96	,,
Tonsillitis (secondary)	,,	1·64	,,
Bronchitis	,,	1·12	,,

Otitis may arise at any stage of the scarlatinal attack after the first few days. Severe cases are much more liable to the complication than mild ones, and in such instances it usually appears earlier in the attack, namely, about the end of the first week of illness. It is an affection of early childhood, the liability decreasing with each year of life. After fifteen years it is very rare, but there is a tendency, even in adults, for old ear mischief to be lighted up by the scarlatinal attack. The influence of sex is negative. This otitis may occur either in the form of a simple inflammation of the external auditory canal, with possibly more or less implication of the membrana tympani, in which case it is but a trivial affection of short duration; or, as is far more common, in the form of an otitis media, followed by a more or less profuse muco-purulent discharge. The collection of inflammatory products pent up in the tympanic cavity, if not let out by incision, will soon relieve itself by rupture of the membrane. That this affection is usually due to an extension of the naso-faucial inflammation along the Eustachian tube, with swelling of the mucous membrane and consequent narrowing of its calibre, would appear to be tolerably certain—at any rate when it arises early in the attack before the throat inflammation has subsided.

The distinctive signs of the affection are pain in the ear, tenderness over the cartilaginous portion of the canal, irritability of temper with more or less fever, followed usually after one to three days by rapid loss of the pain, tenderness and fever on the appearance of the discharge. The glands immediately beneath the ear are usually enlarged and tender, and may remain so for several days. They occasionally suppurate. The discharge usually ceases after from two to four weeks' treatment, and the perforation rapidly heals; but in exceptional instances cure may not be effected in less than three or four months.

In some cases an inflammatory swelling appears over the mastoid bone, attended with a rise of temperature and intense tenderness. The swelling gives rise to more or less projection of the external ear. It is limited above by the temporal ridge, to which the fascia is bound down, and by its extension forwards leads to considerable œdema of the eyelids on the same side. It will be found to depend either upon a periadenitis which often suppurates, originating in one or more of the posterior auricular glands, or, as is more common, upon the formation of a subperiosteal abscess connected with carious bone and the presence of pus within the mastoid cells. In those cases of subperiosteal abscess, in which these parts are sound, it is possible that pus may have found its way from the middle ear by effecting a passage between the cartilage and the bony portion of the auditory canal. The firmness with which the thick fascia in the temporo-zygomatic region is bound down may effectually prevent the appearance of any œdema in this situation; and it is in some cases hard to realise that the source of what appears to be an independent œdema of the eyelids is really to be found, either in an inflammation of the middle ear, or of the mastoid bone on the same side. When suppuration has actually occurred in the swelling a definite ring of softening can be usually detected over the subjacent bone at a point immediately behind the external ear. If the swelling be situated either anterior to or below the auditory meatus it is always superficial, and depends upon a suppurating auricular gland.

In those somewhat exceptional instances of otitis media, in which extension to the mastoid cells occurs during convalescence from an attack of scarlet fever, the symptoms are of considerable urgency; especially if no relief of tension is possible at the surface of the bone. Minute interstices in the osseous tissue of the mastoid, by means of which a communication between the interior and the subperiosteal surface is possible, exist in all subjects, but their patency and freedom of communication vary in different individuals, as does also the depth at which the antrum may lie from the surface.

The signs of *suppuration of the mastoid cells*—a condition which in young children is synonymous with empyema of the mastoid antrum—are briefly as follows:—Pain, and more or less tenderness, the latter occasionally intense, are complained of in the bone, together with local œdema and usually some redness of skin. The discharge, though rarely completely arrested, is often diminished in quantity. The temperature, which may rise to 105° or more, shows wide fluctuations, and is often accompanied by occasional rigors. The pulse is rapid and excitable, and in some cases markedly irregular. Great restlessness and irritability are present, and vomiting is common. The symptoms may rapidly abate and the discharge become more free, but they usually soon recur, often beginning with a rigor, and, unless relieved by operation, the case as a rule ends fatally by meningitis, or after a more protracted and irregular course. One case I have seen in which the temperature reached 112° before death. The general symptoms of suppuration of the mastoid cells are not unlike those seen at an early stage in some cases of acute nephritis.

It is well known that meningitis, intracranial abscess, both subdural and within the substance of the temporo-sphenoidal lobe or cerebellum, and general pyæmia, are all liable to supervene in cases of chronic middle ear disease. These conditions, like septic thrombosis of the lateral sinus, are events too remote to be considered here. The chance of their appearance in hospital-treated cases of scarlet fever should not be great; they are more prone to arise in patients who have passed through an attack of scarlet fever in their own homes, and in whom a septic condition of the middle ear has been allowed to establish itself.

Although I have never met with a case in which sinus thrombosis was definitely known to have supervened within a few months of the scarlatinal attack, I have on two occasions, post-mortem, found pus in the sigmoid groove between the sinus and its bony wall, the pus having worked its way backwards from the antrum which was full of it. The fact that it is by no means infrequent to find true pus in the mastoid antrum after death, though its presence may have never been even suspected during life, would certainly suggest that its occurrence is much more frequent in cases of the septic type than is generally supposed.

Adenitis is a somewhat rapid swelling of one or more of the cervical glands, either behind the jaw or placed deeper under the sterno-mastoid, occurring during the stage of convalescence; the temperature having been normal perhaps for from one to three weeks. It is attended with a fresh rise of temperature, which remains elevated for a longer or shorter period, dependent on whether the gland proceeds to suppuration, or, as more frequently occurs, resolves. In the latter case the temperature usually returns to normal within three days. Its fall, like its rise, is frequently somewhat sudden.

The gland swelling which occurs early in the scarlatinal attack in connection with an inflamed throat is not here referred to. This, which in some degree is common to all cases with any throat affection worth speaking of, may vary from a very slight glandular fulness up to the most severe state of gland infiltration, attended with enormous swelling of neck and a profuse muco-purulent rhinorrhœa, all of which are directly dependent upon a septic ulceration of the fauces and tonsils. This state is really one of septic adeno-cellulitis; and such cases are not complications but part and parcel of a severe attack in its acute stage: moreover they are due to an obvious primary cause, like the glandular swelling directly consequent upon pediculi or eczema capitis.

I refer rather to a primary pyrexial adenitis, occurring at a late stage of the disease, and unconnected, so far as can be seen, with any local exciting cause. In its pathology it would appear to be more directly related to those cases of sudden gland swelling which arise as a result of what is called, for want of a better name, "taking a chill," whatever that really may be. These cases of adenitis are often seen to arise in groups about the same time in patients located in different parts of the hospital. They are met with in about equal frequency at all times of the year, and show no clear connection with either cold, damp, diet or habits. Their occurrence in groups appears to suggest some widespread causative influence, such as some varying atmospheric or soil condition. It is more often met with in patients the subject of albuminuria, especially in those who have a distinct nephritis. The complication is rarely met with after the fourth week of illness, it is more common in the second than the third, and in the third than the fourth. It is far more common before the age of puberty than afterwards, and is perhaps more frequent after severe than after mild attacks. It bears no relation to sex, and always terminates in recovery. About one-third of the cases suppurate; and it is always wise, in opening such collection, to make use of a drainage-tube in view of the tendency to residual abscess.

Articular Rheumatism.—Rheumatism, of sufficient intensity to give rise to elevation of temperature, pain, tenderness, and distinct effusion into the joints, is a common complication. Its most frequent seat is the smaller rather than the larger joints: the arms suffer more frequently than the legs; the hands and wrists, than the elbows or shoulders; and the ankles, than the knees or hips. Most frequently of all it appears in the metacarpo-phalangeal joints and the wrists, but evinces a certain tendency to migrate. There are good reasons why it should be regarded as pathologically akin to ordinary acute rheumatism, though differing in certain respects. It is very prone to arise in persons who have been subject to antecedent attacks of acute rheumatism, although such persons are in the minority. It shows, in a less degree, the same tendency to move from joint to joint, and it is readily amenable in most instances to the action of salicine and the salicylates. On the other hand, it is less severe than ordinary acute rheumatism, its natural bent being more towards recovery; it is unattended with the acid perspirations and the creamy, furred tongue so characteristic of that condition; and it shows less tendency to affect the fibrous tissues of the heart or pericardium. Moreover, the joints are more prone to take on a suppurative action, leading to a condition of pyæmia, than in the ordinary rheumatic process. This so-called "Scarlatinal Pyæmia" frequently yields to appropriate surgical treatment.

Scarlatinal rheumatism is far more common in adults and in older children than in young ones, and affects females in a much larger proportion than males. It arises independently of season or temperature, being as common in the summer and early autumn months as in the colder seasons. Its time of onset is remarkably constant, viz. the fifth, sixth, or seventh day of illness, at the time when the rash is just disappearing and the temperature falling to normal. It is more common in severe attacks than mild ones—in cases characterised by an intense rash and copious peeling—and it is in cases such as these, especially if of the septic type with ulcerated fauces, that the joint affection has a tendency to assume the suppurative form. The prognosis in ordinary cases is good, the affection usually yielding readily to treatment with the salicine compounds. The cardiac structures are rarely involved at the time, probably in less than 3 per cent. In those exceptional instances in which the joints suppurate, the elbow, knee, and sterno-clavicular joints seem to be earliest and most frequently affected. Early evacuation of the joint, with antiseptic irrigation, is usually followed by the best results.

Albuminuria.—Under this heading in the foregoing table cases of acute nephritis are not included, nor those in which but a faint and transient cloud of albumin was noted for less than three consecutive days. The urines during normal convalescence, unless any special indication existed, were only tested twice a week; and in infants it was not always possible to examine the urine with absolute regularity.

The test employed was a delicate one, viz. the addition to the urine of an equal bulk of a saturated solution of picric acid, *plus* one drop of acetic acid to the drachm. A good plan in systematic testing for albumin is to employ the cold nitric acid test, by way of confirmation, to any urines giving a positive result with the picric acid. In this way the possible fallacies are reduced by the exclusion of peptones and mucin.

The incidence of scarlatinal albuminuria in patients treated in hospital wards is not so great as is usually supposed. It must be remembered, however, that the inclusion of three or four beaten up eggs in the diet of an adult will produce albuminuria by simple diffusion. In this series the amount of easily diffusible albumin given in the diet was not sufficient to yield signs of its presence in the urine, so that instances of albuminuria due to this cause were not to be expected. I believe that the albuminuria in which a faint cloud only could be obtained with picric acid for less than three consecutive days may be safely absolved from any prognostic significance: they do not show any tendency to recurrence, nor does the urine on careful microscopical examination yield evidence of any renal product. But in albuminuria of greater degree, it is admittedly a difficult thing to draw a distinct line of demarcation between that which does and that which does not indicate acute nephritis, because cases of acute nephritis vary so widely in the severity and constancy of their symptoms. Nor must it be forgotten that certain very exceptional cases of nephritis are met with in which the urine, even on careful daily examination, has shown no sign of albumin, though the clinical signs and post-mortem appearances are characteristic of the disease. Three such instances have occurred in my own experience. Pathologically, the difficulty of separating the two states is still greater, because the constancy with which kidney changes are present in cases of uncomplicated scarlet fever is a matter of dispute; and the opportunity of verifying the presence of substantive disease of the kidney in cases of simple albuminaria, so-called, is of rare occurrence.

I hold strongly to the belief that, although changes in the renal tissue are by no means necessarily present in an ordinary attack of scarlatina, yet simple albuminuria of any degree and acute nephritis, when they supervene, are due essentially to the same morbid process, varying simply in intensity, or in the vulnerability of the kidney in the particular subject. The assumption that a simple albuminuria and a nephritis are both the expression of the same morbid action, varying mainly if not entirely in respect of degree, is supported by certain facts of their development. Their relative prevalence in a particular outbreak or in a particular ward is in agreement; they both tend to arise under the same conditions of environment: deficient ventilation, overcrowding of wards, especially with acute cases, climatic changes, chiefly in respect to atmospheric humidity, all have an apparent influence in determining the appearance of both. It may be noticed in passing that cold *per se* seems to be without influence; but cold in conjunction with damp is often followed by the appearance of fresh cases. They both show a tendency to develop at the same stage of the illness, viz. during the second and third weeks (most frequently the tenth to the twenty-first day).

The age liability also is in agreement, the susceptibility to both affections being fairly constant from the second year of life to the fifteenth, after which age cases of simple albuminuria are relatively more common than those of acute nephritis. The fact also that there is as great a tendency for cases of simple albuminuria to end in acute nephritis as there is for cases of acute nephritis, if neglected, to relapse, is additional evidence in the same direction.

That kidney disturbance is less frequently met with in cases of scarlet fever treated in hospital than in those treated in their own homes, at any rate amongst the poorer classes, is very probable; and it is quite possible that this is in part referable to the fact that during their illness the patients are kept under more favourable atmospheric conditions: moreover, the action of the skin is encouraged by the employment of frequent and regular warm baths, begun directly the temperature has reached the normal, and continued during the stage at which the renal susceptibility is at its greatest.

Cases of "postural" or "cyclic" albuminuria are occasionally met with, and it is probable that their pathology is of a more complex nature.[1] The very large proportion of patients who have been the subjects of simple albuminuria completely lose their albumin in a few weeks. I cannot call to mind an instance of a scarlatinal patient being discharged with albumin in the urine who had not previously suffered from a definite attack of acute nephritis.

Acute Nephritis.—Although, as we have seen, it is not easy to draw a distinction between certain mild cases of nephritis and those of simple albuminuria, yet in a certain number the symptoms of a profound inflammatory affection of the kidney are sufficiently pronounced to warrant the designation "acute nephritis." They are not, however, so numerous as those falling under the head of "simple albuminuria." If we put the two classes together as simply an expression in different degree of the same diseased action, the percentage of cases showing renal affection in this series of 4015 attacks comes out at 7·69.

The symptoms of onset in the majority of cases are sudden and pronounced, comprising headache, vomiting, often a rigor, drowsiness, sudden elevation of temperature to 103° or 104°, the appearance of blood and albumin in the urine, and a greater or less degree of suppression. The period of suppression corresponds usually with the febrile stage, and is seldom at its height until the second or third day, by which time the excretion may have fallen to three or four ounces, often with frequent desire to pass water. The skin is hot and dry, the pulse excitable, the respiration rapid, the tongue dry, and by this time there is usually evidence of slight anasarca, best seen in the face, loins, hands, and feet. The febrile stage usually lasts from three to six days, and the temperature is very variable, often fluctuating between 97° and 102° or 104° several times during this period. It is hardly ever sustained for twenty-four hours at a stretch, but is of a strikingly "spiked" character when charted. The pulse, which has been variable both in rhythm and strength, not infrequently becomes preternaturally slow and full towards the end of the week, by which time the urine is passed in greater quantity. In a smaller proportion of cases the onset is much more gradual; the febrile signs, if present at all, being preceded by the appearance and gradual increase of albuminuria for several days. In these cases the condition does not at any time look so alarming, but the prognosis is less favourable, and when recovery ensues, it is usually longer deferred.

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[1] Some convalescents show no sign of albumin till they get up, and the albumin is lost at once on returning to the recumbent posture. In one boy the albumin could be made to vary from 0 to ½ by getting him up for half an hour; it invariably fell to a trace on returning to bed, or even lying down in his clothes for an equal period. This alternation could be repeated at will for two months. Slight variations of the kind are not uncommon. Whether such patients eventually show signs of kidney disease I cannot say.—F. F. C.

Hæmaturia in some degree is a constant symptom, but anasarca to any extent is rare. The nephritis is often associated with adenitis, and not infrequently with rheumatism, which usually precedes it. Acute nephritis, like simple albuminuria, most frequently arises during the latter part of the second and the third week. In a small number of cases it appears as late as the fourth week. It is most frequent in cold, damp, or "muggy" weather. All ages are liable to it, but it is less frequent after puberty. Sex seems to be without influence up to fifteen years, but at a later age males are more liable. Nephritis is as common after mild attacks of undoubted scarlet fever as after severe ones.

The prognosis in nephritis arising in patients while in hospital is good. Of 2148 consecutive admissions during the year 1892 into the South-Western Hospital, 65 developed nephritis in the hospital, of which 4 died, and 2 were discharged with chronic albuminuria after six months' treatment; whereas of 12 patients who were admitted suffering from scarlatinal nephritis, 4 died, and 3 were discharged with chronic albuminuria after a prolonged residence. Now, although as regards the latter class the results were more than usually unfavourable, yet the contrast is striking, and confirms results previously noted in a much larger series of cases. Death in scarlatinal nephritis is almost invariably due to the advent of one of the three following conditions, arranged in order of frequency—uræmia, suppurative inflammations, acute pulmonary œdema. Of these the last is by far the most dangerous to life.

Eczema.—The parts most often affected are the face, the scalp, and the ears. In the latter case it is usually found at the junction of the ear with the side of the head, within the groove of the helix, and round the external auditory meatus, where it is directly dependent on the irritant effect of an otorrhœa. The same condition is noticed round the external nares and on the upper lip, where also it is usually connected with a discharge from the nasal passages. It commonly assumes the impetiginous form, and is greatly aggravated if the child be allowed to pick the affected spots. In this way it may be transmitted to the chin or any other part. It is far more frequent in young children than in older patients, and more often affects those on a meat diet. Not infrequently it is associated with ringworm of the scalp. Eczema is more common in the winter months than in the warmer seasons, and is very liable to supervene in children whose faces have become chapped by previous exposure. Although all young children are to a considerable extent liable to impetiginous eczema, yet it arises far more frequently in connection with scarlatina than with any other infectious disease.

Ulcerative Stomatitis.—The condition here referred to varies enormously in the severity of its manifestations. It most frequently begins as a simple sponginess of gum, often in connection with a carious tooth. Ulceration then appears at its free border, with a tendency to bleed on being touched. The diseased action next tends to spread laterally, and affects either the adjacent border of the tongue or the mucous surface of the cheek or lip. The disease may stop at this point, and remain limited to the appearance of a few shallow ulcers with an angry-looking margin and a grayish floor, in conjunction with the spongy ulcerated condition of the gum before referred to. Such cases are invariably attended with a moist and somewhat brownish coating to the tongue, a certain degree of salivation with enlargement of the submaxillary lymphatics, and a distinctive fœtor of the breath. They do not present any rise of temperature or serious constitutional disturbance. In other cases, however, things are very different. The ulceration of the gums rapidly spreads and assumes a necrotic form; the teeth become loose or fall out; the ulcers on the tongue, lip, and cheek take on a fungating character, or actual sloughs may appear in the latter situation, and eventually, if the case be left to itself, involve the whole thickness of the cheek. A black incrustation forms on the teeth, and the temperature may be raised several degrees with signs of profound constitutional depression. Cases of this degree of severity, deserving the name *noma*, are of rare occurrence, and if taken early may be cured by energetic treatment.

Ulcerative stomatitis complicating scarlet fever is a disease of young children, being virtually unknown after the age of puberty. It shows no special connection with either sex or season, but is most common in strumous subjects, and in those who are suffering from, or who have recently had measles.

There is a distinct disposition in this diseased mucous membrane to become infected with diphtheria; I have seen this complication supervene in three cases of ulcerative stomatitis arising in the ordinary manner, and ultimately prove fatal by involvement of the larynx. The affection is eminently contagious.

Secondary tonsillitis is very much more frequent in adults and older children, in females, and in those who have previously been subject to it. Severity of attack, damp weather, and overcrowding of wards with acute cases exert a marked influence. It is rarely severe, and suppuration is infrequent. The liability seems to be about equal at all stages of convalescence.

Bronchitis.—This affection when appearing in a scarlatinal patient presents nothing unusual in its characters. It is most frequent during cold weather, chiefly affecting young children, in whom it usually appears at an early stage of the illness. It is rarely of any prognostic importance except in children specially susceptible in virtue of previous attacks.

Among the rarer conditions incidental to convalescence, which may not indeed be directly connected with the action of the scarlatinal poison, may be mentioned urticaria, herpes, psoriasis, abscess, cellulitis, boils and ophthalmia. It should also be remembered that scarlet fever convalescents are very liable to take the infection of any other member of the group to which they may be exposed, particularly that of diphtheria.

The wide variation in liability to the different affections in connection with age is well brought out in the following table, which deals with their percentage incidence amongst 2078 cases completed in the South-Western Fever Hospital during the year 1892 :—

TABLE V.—Incidence of Complications at different Age Periods amongst 2078 cases of Scarlet Fever.

	0–4.	5–9.	10–14.	15–19.	Over 20.	All ages.
Otitis	18·5	10·1	4·1	0·7	2·5	9·91
Adenitis	11·7	10·0	8·3	1·4	2·5	9·19
Rheumatism . . .	0·4	4·5	9·0	9·9	13·6	5·53
Albuminuria . . .	4·4	3·2	2·0	5·6	5·1	3·52
Nephritis	3·6	3·7	3·6	0·7	0·8	3·32
Eczema	3·8	1·3	0·6	0·0	0·0	1·58
Tonsillitis (secondary) .	0·2	1·1	2·9	1·4	2·5	1·44
Ulcerative stomatitis . .	3·4	1·1	0·4	0·7	0·0	1·39
Alb. and nephritis combined	8·0	6·9	5·6	6·3	5·9	6·83

The influence of sex in respect to most of the complications is but slight, but some variation is seen in the case of tonsillitis and rheumatism, females being more liable than males in the proportion of 3 to 1 and 2 to 1 respectively.

Post-Scarlatinal Diphtheria.—As to the factors concerned in the development of this, the gravest complication to which the scarlet fever convalescent is liable, considerable uncertainty prevails. Though any stage of the scarlatinal attack may be complicated by the appearance of diphtheria, it is during convalescence that the large majority of cases arise. It occurs more frequently in hospital-treated patients than in those who remain at home, at any rate among the better classes. This fact suggests that its incidence is dependent upon conditions which are to a great extent special to hospital life. Now, experience shows that its frequency varies in different hospitals, in different wards, and at different times in the same hospital. Many suggestions have been offered to explain its appearance.

The presence in a scarlet fever ward of a previous case of diphtheria, which, perhaps owing to its extreme mildness, may have entirely escaped observation, must doubtless be admitted as a possible source of infection in certain cases; although a recognised case of diphtheria rarely, if ever, gives rise to other cases in a scarlet fever ward, if that ward be properly ventilated and provided with sufficient floor space per bed. The facts of the appearance of post-scarlatinal diphtheria in certain hospitals are frequently much more suggestive of the operation of some more general and widespread influence, such as an atmospheric or soil condition. Cases of post-scarlatinal diphtheria are frequently observed to arise in groups of two, three, or more, almost simultaneously or in close succession, in different wards of a large hospital, wards which are not only widely separated, but which may have no administrative factor in common, with the exception of the food supplies which can be clearly absolved. Such outbreaks have not infrequently arisen in seasons characterised by a high degree of atmospheric humidity, dependent upon previous rainfall and consequent dampness of soil. The incidence of the disease is for the most part greatest in wards surrounded with grass or other vegetation growing in a clay soil; indeed, the moisture-retaining character of the actual surface would seem to be of greater importance than the subsoil drainage, whether natural or artificial.

The possibility of mediate infection by means of linen, books, toys, etc., or the persons of attendants on the sick, must not be overlooked, nor must it be forgotten that in certain exceptional instances a connection has been conclusively established between outbreaks of diphtheria and defective drainage. I have, however, come across cases in which it was possible to eliminate all such influences, in so far as they are capable of elimination. Statistics, moreover, go to prove that the incidence of the affection bears no relation to the proximity of a diphtheria ward. At one hospital which has enjoyed a comparative immunity from post-scarlatinal diphtheria, its incidence has been more than twice as frequent in wooden huts, deficient in floor space per bed, than in brick-built wards with an ample provision; and its appearance has been strikingly shown to follow in the wake of even temporary overcrowding of wards in other respects satisfactory. In the treatment of scarlet fever it is most necessary that the heating appliances in a ward should be capable of maintaining the air at a satisfactory degree of warmth and dryness, and at the same time permit of ample direct ventilation. The floor space per bed should on no account be reduced below 144 square feet, and the airing court surrounding the ward should have a gravel surface, or better still, be laid with tar paving. Were these points insisted upon in the construction of all fever hospitals, there is little doubt that the appearance of post-scarlatinal diphtheria would be considerably reduced, assuming due care to be exercised in respect to their administration.

The incidence of post-scarlatinal diphtheria amongst 14,548 cases of scarlet fever admitted into the Asylums Board Hospitals during the year 1893 was 1·4 per cent, of which 58·3 per cent were fatal. In exceptional cases its incidence in a single hospital has risen to above 2 per cent of the admissions.

There is nothing, either clinically or bacteriologically, to distinguish post-scarlatinal diphtheria from the independent disease, except in respect to its unduly high mortality. While the mortality in the series under consideration was 58·3 per cent, that of the diphtheria admissions in the same period, numbering 2848 cases, was only 30·4 per cent. This excessive mortality is in great part dependent upon the fact that more than half of the attacks occurred in children under five years of age, who, in ordinary diphtheria, die at the rate of 53·8 per cent in the public fever hospitals of London; at this age period in the cases under consideration the mortality reached the height of 74·7 per cent. Moreover, having regard to the fact that in 75 per cent of these children the disease assumed the laryngeal form, it may be confidently stated that the excessive mortality in post-scarlatinal diphtheria is mainly owing to a special tendency of the disease to affect the respiratory passages. The results following tracheotomy, again, are not so favourable as when the operation is performed in cases of independent diphtheria.

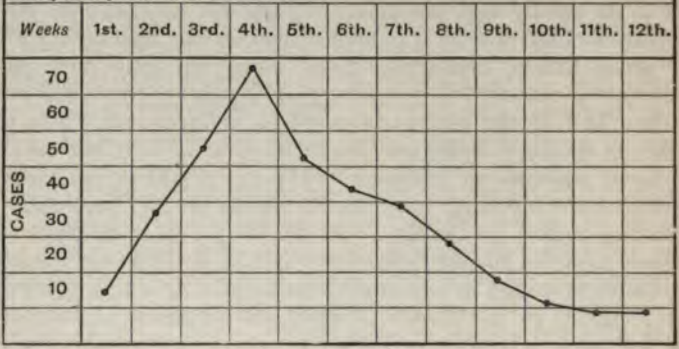
The following table deals with the time of incidence of the diphtheritic complication in 408 cases:—

TABLE VI.—Time of onset in 408 cases of Post-Scarlatinal Diphtheria.

Week.	Under Five Years.	Over Five Years.	Total.	Percentage of total cases.
1	5	6	11	2·69
2	20	16	36	8·82
3	32	23	55	13·48
4	53	24	77	18·87
5	35	19	54	13·23
6	26	20	46	11·27
7	22	16	38	9·31
8	21	6	27	6·61
9	9	9	18	4·41
10	8	5	13	3·18
11	4	5	9	2·20
12	4	5	9	2·20
later than 12th	12	3	15	3·67
Total	251	157	408	100·

The variation in the time of incidence is best seen if the above numbers are shown in the form of a chart, and, since the rise and fall of the curve is both regular and progressive, it may be fairly taken as an expression of the varying susceptibility to the disorder at different periods of the scarlatinal attack. This tends to show in the most striking manner that susceptibility is at its maximum during the course of the fourth week.

Chart C. *Showing variation in liability to Post-Scarlatinal Diphtheria at different stages of convalescence from Scarlet Fever. Compiled from 408 Cases.*



Relapse.—A true relapse not infrequently occurs in scarlet fever—a state in which all the characteristic features of the disease are simply repeated in a person who has recently passed through one attack. As a rule the severity of the relapse is in inverse ratio to that of the primary affection. Few relapses are fatal, although they are not infrequently severe. The relapse may occur at any stage of the disease after the middle of the second week. Any attempt to draw a distinction between a relapse and a second attack is purely arbitrary. In the former instance it simply means that the immunity conferred by an original attack is not sufficiently prolonged to protect a person from the contagion which is being given off from his own person. Relapses are more common in hospital patients than in those treated at home, as the infection in the air of a fever ward is constantly being renewed by the admission of fresh cases; consequently a person whose immunity is short-lived is far more likely to fall again a victim to the disease. In this case the "relapse" should more properly be called a "second attack." Amongst some 12,000 cases of scarlet fever which have come under my observation, a true relapse or second attack appeared in ·7 per cent. In one instance a young woman had three definite attacks of scarlet fever within a period of three months; in the last of these she died.

If a person have once passed safely out of the infected environment of a primary attack, he very rarely falls again a victim to the disease within the four or five years immediately following his recovery. I remember three such instances only in which the first attack was beyond dispute, but a second attack arising after a long interval is not very infrequent.

XIII. Pathology.—Scarlet fever is in all probability dependent upon the vital activity of some micro-organism. In recent years several observers have attributed a specific causal relationship to some one or other of the various forms of bacterial life which have been found in the human body, but it must be confessed that one only has any claim to recognition. The organism I refer to is a micrococcus, or more strictly a streptococcus as it occurs in pairs or short chains, which has been isolated by Dr. Klein from the blood and tissues of persons suffering from scarlet fever. It was in connection with an investigation instituted by the Local Government Board in 1885, into the cause of an outbreak of scarlet fever in the Marylebone district, that Dr. Klein was first led to believe in the specificity of this microbe. The epidemic was found by Mr. Wynter Blyth to be limited to the consumers of the milk supplied from a dairy-farm at Hendon. Further, it was conclusively shown by Mr. Power that the suspected milk had been exclusively derived from certain cows on this farm which were the subjects of a peculiar disease, and that persons living in other parts of London, who had likewise consumed this milk, were also attacked with scarlet fever. The most prominent features of this cow disease were an ulcerative eruption on the teats and udder, attended with distinctive lesions in some of the viscera. From these ulcers and from the diseased portions of the viscera Klein satisfactorily isolated the streptococcus which he found in human scarlet fever, and which he holds to be the specific cause of the disease.

It is contended by many practised bacteriologists that Dr. Klein's streptococcus of scarlatina, like that of erysipelas and puerperal septicemia, is neither more nor less than the streptococcus pyogenes under a different name. Klein, however, while admitting that the scarlatinal streptococcus is practically indistinguishable from the streptococcus pyogenes either morphologically or in its appearance under cultivation, asserts that by careful study of its biological characters it can be satisfactorily distinguished. In support of this statement he seems to rely chiefly on the fact that the results of its inoculation into the lower animals cannot be procured with the streptococcus pyogenes. It cannot be denied that Klein's position is consistent. He has proved that definite lesions, resembling those found in certain cases of scarlet fever, are produced in cattle and rodents by the introduction of an organism derived from the blood and tissues of persons suffering from scarlet fever, that this organism can be recovered by cultivation, and that it will set up the same disease if injected into other animals. But Klein has not succeeded, in the first place, in showing—and here is the weak link in a chain of evidence in other respects excellent—that the strictly scarlatinal symptoms in human scarlatina are dependent upon the presence of this particular micro-organism; and, secondly, that an organism obtained from an animal suffering from a disease undoubtedly set up by the injection of material derived from human scarlet fever, is capable of originating true scarlet fever if introduced into the human body. The latter point is incapable of demonstration, as the experiment cannot be made, but the first is deserving of very careful consideration.

In the large majority of severe cases of scarlet fever we have undoubted clinical evidence of the presence of a septic element in the attack—in many instances leading to the formation of abscesses in various parts, and in a few running on to definite pyæmia. In such cases it would be not unreasonable to expect the presence of the streptococcus pyogenes in some parts of the body. In the ulcerated faucial mucous membrane, in the infiltrated glands, in the various abscesses, and in the discharge from an otitis media, its presence may be demonstrated with tolerable certainty. Fraenkel and Freudenberg found it in the blood of three persons who were the subject of secondary infections. Lenhartz ascertained its presence in the blood of a patient affected with glandular suppuration. Raskin, though successful in finding the organism in cases complicated with suppuration, in simple cases was unable to detect its presence in the blood in a single instance.

The inference that the streptococcus scarlatinæ described by Klein is concerned simply with the septic element in a severe case, and that the bovine disease artificially produced bears a corresponding relation, is undoubtedly supported by the fact that the minute visceral lesions which have been described by Klein in twenty-three fatal cases of scarlet fever have not been proved to be present in a single mild case in which death happened from some cause unconnected with the scarlatinal attack. Moreover, if the lesions which he has so carefully described in these cases were dependent upon a septic element in the attack, one would not be surprised at the similarity revealed by a microscopical examination of the organs of an animal which had been inoculated with the same septic microbe.

Even less definite is our present knowledge as to the nature of any chemical body concerned in the production of the symptoms of the disease. A toxine has been extracted from the urine, of which the chemical composition has been ascertained, and to which the name "Scarlatinine" has been given. Its poisonous nature has been proved by injection into some of the lower animals, but the effects have been in no way suggestive of the phenomena of scarlet fever, nor is there any valid reason for regarding it as anything more than a product of the scarlatinal process. It is readily destroyed and rendered inert by oxidation.

Whether the multiplication of the scarlatinal poison takes place in the blood, or in any particular organ or tissue, is unknown. Because the throat and the skin are the parts earliest and most severely affected by the scarlatinal process, it has been assumed that they may constitute a nidus for the special multiplication of the poison. It is quite probable that such may be true of the throat in respect of the septic organisms concerned in bringing about the sapræmic condition which obtains in so large a proportion of bad attacks, and that the faucial tissues may constitute a focus from which secondary infections of a suppurative nature are derived. The sequence of events observed clinically, and the beneficial results of vigorous local treatment, lend support to this view. But as regards the peculiar scarlatinal factor, the supposition is strongly negatived by the fact that the most rapidly fatal cases of all—namely, those of the toxic variety—are usually unattended with severe faucial affection; and in some of them the eruption, if not entirely suppressed, is ill-defined and of limited distribution. In all probability it is the blood which provides the field for the multiplication of the virus, as would seem to be the case in typhus and relapsing fever.

The scarlatinal rash is characterised anatomically by an active hyperæmia of the cutis vera, attended with a certain degree of capillary stagnation and considerable inflammatory œdema. Transudation of leucocytes, and of a variable amount of blood pigment into the surrounding tissue, next occurs, attended with a rapid proliferation of the cells of the Malpighian layer, which becomes considerably thickened in consequence.

Desquamation is brought about by the effusion of serum between the cells of the epidermal layers just superficial to the rete mucosum, in virtue of which their mutual cohesion is weakened, and actual separation occurs at the point of effusion. This is best marked in those papules which actually become vesicular. When the fluid contents have dried up, their delicate investments soon become ruptured in the centre, leaving a series of pinholes from which peeling extends centrifugally. The eruptive hyperæmia also induces a trophic change in the rete mucosum, which is characterised by excessive proliferation of its component cells. In this way the shed epithelium is rapidly renewed.

Although the hair follicles are implicated to a considerable extent in the inflammatory process, it is a mistake to regard them as necessarily concerned in determining the minute papular elevations of the cutis which are so characteristic a feature of the eruption. Many of these unquestionably correspond in position with the inflamed follicles, but the greater number are quite independent of them, being numerically in considerable excess. Moreover, the surfaces of extensive cicatrices which are entirely destitute of hair follicles are occasionally observed to be more or less covered with punctiform elevations.

The faucial inflammation in simple cases is characterised by inflammatory hyperæmia of the mucous membrane, attended with an accumulation of leucocytes in its deeper parts. Proliferation and degenerative changes in the epithelial cells occur, and the exudation of fibrinous lymph. In more severe cases the superficial layers of the epithelium perish, and, by an extension of the process, more or less ulceration of the mucous membrane results.

The tonsils share in the inflammation to a variable extent; in some cases a slight degree of swelling, accompanied by adenoid proliferation and an increase of the follicular secretion, is all that occurs. In those of the septic type, on the other hand, extensive ulceration usually takes place, and small foci of suppuration may appear in the substance of the tonsil. The organs may slough *en masse*, and the necrosis by its extension result in widespread destruction of the pillars of the fauces, the velum palati, and the tissues comprising the upper part of the larynx. In such cases the ulcerated surface is found crowded with putrefactive organisms, which also invade the lymphatics leading down to the subjacent glands. These latter are infiltrated with inflammatory products, and not infrequently suppuration occurs in their substance or in the surrounding cellular tissue. In addition to other micrococci concerned in purulent infection the presence of the streptococcus pyogenes can almost invariably be demonstrated in the lymphatics and neighbouring tissues.

It must be confessed that to the naked eye the post-mortem appearances in a fatal case of scarlet fever are neither striking nor constant. They necessarily vary with the type of attack, the stage at which death occurred, and the presence or absence of any definite complication.

Rigor mortis is usually well marked. In toxic attacks decomposition sets in early, and is remarkably rapid. In such cases cadaveric lividity usually appears before death. The blood is dark in colour, thin, and coagulates imperfectly. The vessel walls usually show a considerable amount of staining, and minute subserous ecchymoses are not uncommon.

The macroscopic appearances of the lungs, liver, spleen, and pancreas are indistinguishable from those seen in persons who have died from other forms of acute fever. The liver is a possible exception, because in scarlet fever it often appears to be more than ordinarily fatty.

The appearance presented by the intestines in some cases of scarlet fever is negative, but in a considerable number an unusual amount of softening of the mucous membrane is present throughout the entire tract. Along with this is often seen uniform swelling and softening of the lymphoid glands. The condition is usually better marked in the solitary glands than in the Peyer's patches; but in some cases both are equally involved. In rare instances this swelling of the glands proceeds to actual ulceration, giving rise to a distinct suggestion of enteric fever; and, like enteric, the affection is commonly seen most distinctly in the lower part of the ileum.

The appearance presented by the kidneys shows considerable variation. In some in which there has been no clinical evidence of nephritis, and even in a certain number in which the symptoms have been well marked, the kidney to the naked eye appears practically normal, with the exception of a somewhat cloudy appearance of the cortex on section, and an undue amount of congestion throughout its substance,—effects which may both be observed in the kidneys of persons who have died from any form of acute fever. The capsule strips readily, leaving a raw-looking surface from which blood exudes freely. In the majority of cases of scarlet fever, however, in which death has occurred early in the disease, the kidney will present the following appearances: The organ is usually somewhat enlarged, sometimes considerably; it is congested, especially in the zone corresponding with the bases of the pyramids, where, and also in the substance of the cortex, minute extravasations of blood are often seen; the stellate veins on the surface are unduly turgid, and the capsule readily separates. The cortical substance on section, and also its denuded surface, is pale, opaque, and of a yellowish tint when washed. The Malpighian capsules are clearly defined on the surface of the organ, and, on section of the somewhat enlarged cortex, appear as minute reddish brown specks; while the branches of the dilated interlobular arteries are seen as small oozing points dotted over the cut surface. If death occur at a somewhat later stage in a case which has been obviously complicated with nephritis, the kidney is usually somewhat increased in size, the swelling being mainly cortical. It is less congested, more opaque, and obviously fatty. The Malpighian tufts may still be defined, both on the denuded surface and on section; but they appear as yellowish dots, and blood can but rarely be seen to exude from them.

In kidney disease of long standing, say from six months to a year, the appearances presented by the organ are those of subacute interstitial nephritis. The kidney is smaller in size, the cortex usually being relatively diminished; the substance is firmer, and the capsule more adherent: no projection of the tufts can be observed on the free surface.

Microscopically, the characters of the scarlatinal kidney are those of a glomerular nephritis.

The appearances are briefly as follows:—

A vascular change occurs, comprising intense congestion of the Malpighian tufts and the smaller vessels of the cortex, attended with hyaline degeneration of their internal coat, and an increase of nuclei in the middle muscular layer. This leads to narrowing and obliteration of their channels in parts, and is especially noticeable at the junction of the afferent vessels with the Malpighian tufts, at which point thrombi are occasionally found. The cells of the supporting connective tissue, and those of the epithelial lining of the capsules, share in the proliferation, so that many of the capsules become so crowded with newly-formed epithelium that their function becomes entirely suspended. Aggregation of round cells or leucocytes next occurs in the connective tissues surrounding the cortical vessels and Malpighian capsules, and to a less extent in the space intervening between the urinary tubules. This accumulation of leucocytes is most marked around the small afferent arterioles at a point immediately before they penetrate the Malpighian capsules. The circulation through the vessels is hindered by the compression to which they are thereby subjected, and the capsules themselves, being involved in the process, ultimately become greatly thickened, and some of them entirely destroyed. Cloudy swelling of the epithelium lining the convoluted tubes, the interior of the Malpighian capsules, and ultimately the straight tubes, sets in at an early date. The tubules eventually become more or less choked by the accumulation of cells in a state of granular and fatty degeneration. Blood too is often effused into their lumen, and many of the tubes become filled with casts composed of either blood-disks or epithelial cells in all stages of degeneration.

If death occur at a later stage in the disease the vascular changes will not be so obvious, but the most striking appearances will be found in the interstitial element, combined with a variable amount of parenchymatous degeneration, proportionate to the intensity of the interstitial affection. The enlargement of the organ is dependent upon a great increase in the number of connective tissue cells throughout the cortex, leading to considerable thickening of the Malpighian capsules, and more or less strangulation of their blood-supply; a certain number of them become obliterated.

The ultimate state, if the integrity of the organ be not in part restored, is characteristic of interstitial nephritis: a greater or less degree of contraction takes place in the interstitial tissue, leading to cortical atrophy, and an abnormal adherence of the capsule. This change in the course of years may lead to a contracted granular kidney.

Considerable diversity of opinion exists as to whether the changes in the kidney above described are necessarily present in all cases of scarlet fever, even in slight degree. Dr. Klein has described the presence of definite glomerular nephritis in twenty-three consecutive cases of scarlet fever, fatal at periods varying from two days to seven weeks; and in all of those in which the organs were examined, he found the renal changes to be associated with certain definite morbid appearances in the liver, spleen, and lymphatic glands (*Trans. Pathol. Soc.* 1877, p. 430). It does not necessarily follow, however, that the changes referred to are present in cases in which the attack is of a mild character. I am able to assert that in one case at least of early scarlet fever, in which death resulted from a cause unconnected with the disease, the kidneys on careful microscopical examination revealed no evidence whatever of glomerular or commencing interstitial nephritis. Excluding those cases in which the albumin is only present as a faint and transient trace, and those in which it would seem to be directly dependent upon the pyrexia, it is well to regard all instances of albuminuria arising during the course of an attack of scarlatina as due to glomerular nephritis of some degree, if only in view of the frequency of its observed occurrence.

Granular degeneration of the muscular tissue of the heart, the so-called acute parenchymatous myocarditis, is usually well marked post-mortem, and may be early visible to the naked eye. It is found to occur with equal frequency in persons dead of other infectious fevers, and probably has no specific relation to the scarlatinal poison.

The same would seem to be true of the secondary suppurations which often arise at a late stage of a septic attack. They usually develop in the glands or connective tissue, but suppurative arthritis and empyema are met with occasionally. (Other manifestations of the scarlatinal poison are dealt with in the section devoted to complications, see p. 150.)

XIV. Treatment.—It must be confessed that all attempts to treat scarlet fever upon specific lines have hitherto been unattended with success. Many and various have been the drugs for which an abortive action has been claimed; usually, it would seem, upon the strength of a few cases which have recovered after their administration. These drugs have been mainly of the antiseptic class, and, when their action has been continuously tried on a large series of cases, their superiority over ordinary methods of treatment has been in no way apparent. It is obvious that thus only can a fair basis of comparison be arrived at.

After placing the patient under the best possible conditions for recovery, treatment should be directed to the relief of distress, and to combat any symptom which by its severity may prejudice the course of the attack. Moreover, by carefully watching the case from its very commencement up to the termination of convalescence, endeavour should be made to anticipate the appearance of any of the numerous complications to which the scarlatinal subject is liable.

1. *General Treatment.*—The patient should be placed in a room which can be freely ventilated, and, at the same time, adequately warmed. This should be effected, if possible, by means of an open fire, the ingress of fresh air being provided for by keeping the top sashes of the windows more or less open both day and night to an extent proportionate to the state of the weather. The air of the room should be kept as dry as possible, and maintained at a temperature of from 56° to 60°. A warm temperature is of more importance during convalescence than it is in the acute stage of the disease. A horse-hair mattress, preferably supported on a chain or wire-wove under-mattress, is the best; and the bed-clothes should be light but warm. During the febrile stage linen should be worn next the skin; but when the temperature has fallen flannel should be substituted, and either it, or a woollen vest, be worn throughout the period of convalescence. The hygiene of the sick-room, though important, does not call for special remark, but should be conducted on rational principles.

So long as fever is present, the surface of the body, at any rate down to the hips, should be washed daily with soap and water, and the action of the skin encouraged by an occasional tepid sponging; due care being taken, of course, to avoid unnecessary exposure of the surface. It is well to "tepid-sponge" the patient every evening as a matter of routine. By this means not only is the tension of the skin lessened and the temperature somewhat reduced, but restlessness is diminished and quiet sleep promoted.

It is usual to give, every three or four hours, even in mild cases, a febrifuge mixture containing either bitartrate, nitrate, or chlorate of potash, and acetate of ammonia, combined with spirits of nitrous ether and a little syrup of orange or lemon peel. A lemonade, composed of lemon juice, bitartrate and chlorate of potash (āā gr. v.-x. ad ℥j.) and soda water, sweetened with sugar, forms a refreshing and useful beverage. The bowels should be encouraged to act daily by means of some mild laxative; for this purpose nothing is better than compound liquorice powder, or the confections of senna and sulphur. In young children an occasional glycerine enema may be sufficient, and, in patients who are getting up, a glass of cold water taken first thing in the morning may be all that is required. A tonic is often indicated during convalescence, preferably one containing iron, in view of the frequent presence of some degree of post-scarlatinal anæmia. The urine should be tested daily for albumin, especially during the second and third weeks. In order to diminish the risk of renal complications, and to facilitate peeling, frequent warm baths should be ordered, starting from the day on which the temperature has fallen to normal; if possible, they should be given daily.

There is no reason why the recent subjects of mild scarlet fever should not be allowed to get up at the end of ten days or a fortnight, provided no complication has arisen, and due care is taken to avoid chill or undue exertion. Young children, however, may with advantage be kept in bed for three weeks after the appearance of the rash, as they are prone to develop some complication during this period. If the weather be dry, and the patient suitably clad, a moderate amount of outdoor exercise is of distinct benefit. Under these circumstances he may be allowed to go out after having been up for two or three days. If the weather be damp, however, and the patient foolish enough to sit about, the practice is then by no means devoid of the risk of renal or glandular complication. For this reason young children should not be allowed to go out of doors unattended.

When the period of quarantine has expired, which should not be less than six weeks, a short residence in the country, if possible at the seaside, will be of permanent value after a severe attack.

The diet during the febrile stage should mainly consist of milk and beaten-up eggs, but the addition of a little soup, beef tea, mutton or chicken broth, and calves' foot jelly, forms a welcome variety, and will do no harm. As soon as the temperature has fallen a more solid diet is permissible; and bread soaked in milk, custard, milk puddings, lightly-boiled eggs, and thin bread and butter, devoid of crust, may be added to the dietary, provided the state of the throat permits of their being swallowed without discomfort. In the course of two or three days the diet may be extended so as to include fish, poultry, and meat.

On purely theoretical grounds it has been contended that nitrogenous food should be withheld during early convalescence from scarlet fever, in order to avoid throwing too much stress upon the kidneys. I am able, however, to assert with considerable confidence that no such risk is found in practice, and that patients will suffer no harm whatever if put on such a dietary as I have described above. There is, moreover, no evidence that nephritis has ever been induced by the administration of a diet containing a moderate amount of nitrogenous food. The desire of the patient himself for solid food is the best criterion of its advisability, and it may be given with confidence as soon as he feels able to swallow it without discomfort. Ripe and succulent fruit may be given at all times throughout the illness. It is not only refreshing, but wholesome.

When there is much swelling or ulceration of the faucial structures, especially if attended with tenderness and infiltration of the submaxillary lymphatics, it may be extremely difficult to prevail upon the patient to take his nourishment; and the same thing is frequently true in cases of the toxic type, the patient being usually restless and refractory, if not actively delirious. In such cases the food should be administered in small quantities, and in as concentrated a form as possible, reliance being then mainly placed upon some of the various meat essences, of which

"Caffyn's Liquor Carnis," "Carnrick's Beef Peptonoids," and raw meat juice, are perhaps the best. These, too, are the only cases in which stimulants are necessary, and even here their use should be cautiously regulated. To a child of five years of age it will be rarely necessary to give brandy in larger quantity than at the rate of one teaspoonful every hour. In prolonged cases of the septic type "Marza Wine" is a preparation of considerable value, consisting, as it does, of meat juice combined with alcohol in a palatable form.

Deglutition in some cases may become practically impossible; it may then be necessary to pass a nasal tube, or feed entirely by the rectum.

2. *Symptomatic Treatment.*—The local treatment of the throat in scarlet fever is of the first importance. In mild attacks, and in those of the toxic variety, nothing more is necessary than to irrigate the fauces every few hours with some mild antiseptic solution, such as boracic acid, bicarbonate of soda, sulphurous acid, or Condy's fluid, applied by means of either a syringe or spray. In adults the throat may be gargled. Local discomfort may be lessened by frequently sucking small pieces of ice, but in some persons more relief is obtained when the fluid nourishment is taken as hot as it can be borne. Hot fomentations or a linseed meal poultice, properly made and evenly applied, should be placed round the throat in all cases when the glands are enlarged and tender. They not only considerably diminish the pain on swallowing, but also appear to favour resolution; moreover, if suppuration threatens, the process seems to be hastened by their application.

In septic cases, however, in which the tonsils have begun to ulcerate, or become coated with exudation, more vigorous methods are called for. Here it is necessary to bring the diseased surface into as healthy a condition as possible by means of some powerful antiseptic solution frequently used, and at the same time to cleanse the naso-faucial passages from offensive accumulations. For this purpose nothing is better, if, indeed, so good, as a strongly acid solution of chlorate of potash containing a large amount of free chlorine. The solution is prepared by pouring strong hydrochloric acid upon powdered chlorate of potash in a large stoppered bottle, and afterwards shaking up with water. The best proportions are—5 minims of the strong acid to 9 grains of the salt, made up to the ounce with water. The resulting solution is of a greenish colour, and smells strongly of chlorine. Both the fauces and nares are thoroughly syringed out every two or three hours according to the severity of the local affection, the syringe best adapted for the purpose being what is known as a four-ounce rubber enema bottle, fitted with a vulcanite nozzle. It is best to employ two syringes at each operation, one being allowed to fill itself in a basin containing about a pint of the solution, while the other one is being used. By the time the latter is empty the other will be ready charged, and there is consequently no loss of time. This latter point is of considerable importance to the patient, as the process is by no means pleasant. This is far and away the best method of dealing with a septic throat, as the solution, which is strongly antiseptic and astringent, is injected in such a manner as to clear the entire naso-faucial tract of its offensive secretions. No amount of gargling, spraying, or swabbing can compare with it in point of efficacy, even if the parts be reached. The patient's head should be held over a basin and the mouth kept open. The solution may be injected with some force, as no harm can be done by a stream of fluid, but sufficient time must be allowed for the patient to get a breath between each squeeze of the syringe. The relief obtained is very great, and even young children, after a short experience, will often willingly submit to its repetition in view of the comfort which follows. By frequently irrigating the diseased surface in this manner the local multiplication of pyogenetic and putrefactive organisms is to a great extent held in check; and consequently, the chance of an extension of the ulceration, or the appearance of any septic changes, is considerably lessened.

If the cellular tissue in the submaxillary or cervical region become the seat of brawny infiltration, it is better at once to make several free incisions into the part affected, rather than to wait for the appearance of definite suppuration. This not only relieves pain and tension, but at the same time provides an escape for the pent-up inflammatory products. In such cases the presence of actual suppuration is often very difficult to determine; indeed it may be absent altogether. Frequently, however, an abscess forms under the sterno-mastoid or beneath the deep cervical fascia. This should be opened at once and a drainage-tube inserted. Afterwards hot fomentations of boracic or carbolic acid should be applied, and changed frequently.

Insomnia, restlessness, and delirium are usually associated with a high temperature. For their relief recourse should be had, in the first place, to cold or tepid sponging. If this fail, opium, sulphonal, or chloralamide may be tried in doses proportionate to the patient's age. The former is frequently beneficial, but should be used with caution after the middle of the second week, when, if any albuminuria be present, its employment is contra-indicated.

The treatment of hyperpyrexia is usually unsatisfactory, as most cases are ultimately fatal. A cold pack should be tried, and its effect carefully watched. Of all drugs, antifebrin, in two to five grain doses, is the best. The doses may be repeated in four hours if the temperature has again risen. No other drug is of equal service, and the combination of antifebrin with the wet pack is sometimes of great value. The use of the graduated bath in scarlatinal hyperpyrexia is recommended by some physicians, but in my hands the remedy has not proved very satisfactory. The temperature of the water at starting should be about 90°, and this should be rapidly reduced until the body-heat has fallen to about 101°.[1]

Diarrhœa, appearing early in the illness, had better be left to itself;

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[1] Packing with bottles of ice, as described in the article on "Hydrotherapeutics" (vol. i. p. 339), has proved successful in more than one case of the kind under my observation. Cold baths are less suitable for children in all maladies.—ED.

but when it complicates the late stage of a severe attack, it must nót be neglected. In such cases Dover's powder is often useful, especially when combined with equal parts of bismuth subnitrate and salicylate of soda. A powder containing two grains of each may be given to a child of five, and the doses can be repeated in four to six hours if necessary.

The treatment of the recognised complications of scarlet fever is important. During recent months, while testing upon a series of cases the value of decoction of cinnamon—for which drug an abortive action had been claimed by Dr. Carne Ross, in cases which could be brought under treatment at a sufficiently early date—I was surprised to find a considerable reduction in the incidence of some of the more common complications of the disease. Indeed, in a series of 200 consecutive cases which were put under this treatment within twenty-four hours of the appearance of the rash, the incidence of adenitis, rheumatism, nephritis, and albuminuria was found to be about 50 per cent below the average. The general death-rate, however, showed no reduction.

Otitis.—The earache, which in some degree is usually present at an early stage, should be treated by gently irrigating the affected ear with water as hot as it can be borne. After this a few minims of laudanum or glycerine of carbolic acid may be dropped into the canal, and a hot fomentation of opium or belladonna applied externally. The instillation of a few drops of a 5 per cent solution of cocaine in liquor atropiæ will sometimes quickly give relief when the former remedies have failed. Now, no doubt we are told to examine with the aural speculum all cases of otitis media in which suppuration is suspected, and, if there be any bulging of the drum, to incise at once; but in the young children who are almost invariably the subjects of the scarlatinal affection, the external canal is so tender and its calibre so small, that not only is the passage of the speculum extremely painful, but a satisfactory inspection is very difficult. In most cases, therefore, it sêems better to rest content with the employment of remedies for the relief of pain. If the membrane rupture spontaneously (which it usually does in a short time), it is doubtful whether any harm results provided the after-treatment is carefully carried out. In many instances the early appearance of the discharge will anticipate surgical interference; indeed, it is not infrequently the first sign of the affection. When otorrhœa is once established it is of paramount importance to keep the middle ear aseptic. With this object the ear should be syringed every three or four hours with some antiseptic solution; the canal should then be carefully dried, and a small piece of cyanide or alembroth wool, sprinkled with iodoform, inserted in the meatus. A good lotion to employ is a saturated solution of boracic acid or one containing a mixture of equal parts of glycerine of carbolic acid and glycerine of borax, in the proportion of one drachm to the ounce of water. If, after a few weeks' treatment, the discharge do not markedly diminish, it is advisable to change the solution for some other possessing greater astringent properties. A good substitute is a lotion of carbolic acid, 1 in 40, containing also two grains to the ounce of either sulphate of zinc or sulphate of copper, varied occasionally by the use of a weak solution of creolin. If the perforation in the drum be large, a few grains of iodoform may be blown up the meatus after syringing, more especially if the discharge be very offensive. At a later stage a few drops of dilute rectified spirit can be dropped into the ear occasionally, the strength being gradually increased from 1 in 4 up to equal parts.

If pain be complained of, attended with tenderness, swelling, and redness of the skin over the mastoid bone, and the temperature at the same time become elevated, a vertical incision should at once be made down to the bone, immediately behind the ear, taking care to divide the periosteum.

In this way a sub-periosteal abscess may be relieved. The bone always feels rough to the probe, but if it be distinctly carious, pus will almost invariably be found in the mastoid antrum. This should be opened at once with a small gouge or rotatory burr; its contents should then be cleared out, all granulation tissue or carious bone scraped away, and the natural channel of communication between the antrum and the tympanic attic at the same time enlarged; due care being taken to avoid injury to the facial nerve. When the parts have been thoroughly cleaned, a solution of carbolic acid or perchloride of mercury should be injected through the antral opening into the middle ear; thence it will escape by means of the external auditory canal, and care should be taken that the head be inclined towards the affected side in order to prevent the fluid from running down the Eustachian tube. Afterwards the cavity in the bone should be packed with a strip of antiseptic gauze soaked in iodoform emulsion, the end being left to hang out of the wound and so provide a drain; the external auditory canal, after being filled with the emulsion, should be lightly packed in the same way, and a gauze and wool dressing firmly applied externally. The dressing should be changed night and morning, and the passages having been thoroughly irrigated with sublimate or carbolic lotion, should afterwards be packed with gauze as before.

If the otorrhœa continue after the mastoid wound has completely healed, it may be necessary to remove the remains of the membrane and the ossicles by way of clearing out the middle ear. This procedure should be adopted if at any time dead bone can be felt on passing a probe into the tympanic cavity.

It is wise, in all cases of otitis media in which an offensive discharge has lasted for more than six months, to explore the mastoid antrum for pus—with the object, primarily, of facilitating irrigation of the middle ear, and ultimately of causing obliteration of the antral cavity. This should always be done, either at the time or as a preliminary step to the complete operation, in cases where dead bone can be felt in the middle ear.[1]

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[1] An excellent description of the foregoing operations and of that necessary for the relief of septic thrombosis of the lateral sinus will be found in M'Ewen's work on the *Pyogenic Diseases of the Brain and Spinal Cord*, published by J. Maclehose and Sons, 1893.

Adenitis.—This affection, when recognised at an early stage, is best treated by the application of a linseed meal poultice, by which means resolution seems to be frequently secured. If suppuration occur the abscess should be at once opened and a drainage-tube inserted. Warm dressings of boracic or carbolic acid should then be applied, and the bowels be regulated by means of a simple purge.

Rheumatism.—In most cases the local application of opium or chloroform and belladonna liniment will be sufficient. The painful joints should be surrounded with warm cotton wool, and a flannel bandage applied, while the affected limbs are supported in as comfortable a position as possible by means of pillows. If the joint affection be severe, and in those rare instances in which the cardiac structures become involved, the free exhibition of the salicylates will be attended with the best results, nor is there any reason to believe that their administration ever affects the kidneys injuriously. If, however, one or more of the joints remain swollen and tender for any length of time, and the temperature show no reduction under full doses of salicylate of soda, a little fluid should be withdrawn from the joint, by means of an aseptic hypodermic syringe, and examined. If it be purulent the joint must be opened, under strictly aseptic conditions. A small incision should be made into the joint on each side, and as the fluid escapes the joint should be irrigated, even to the point of distension, with a 1 in 20 solution of carbolic acid. This should be allowed to escape, and the openings closed by means of a small piece of antiseptic gauze soaked in collodion. Firm but elastic pressure should then be exerted upon the joint by means of a bandage tightly applied over several layers of alembroth wool, and the limb placed upon a splint. In many cases this treatment was entirely successful, no re-collection of pus having ensued. Gentle passive movement was allowed at the end of two or three weeks, and a sound joint was the result in all. This sub-pyæmic condition seems invariably to have supervened upon an affection which, though originally rheumatic, did not prove amenable to the action of the salicylates.

Nephritis and Albuminuria.—When the renal inflammation takes an acute form, as evidenced by the severity of the constitutional disturbance and the degree of urinary suppression, the treatment should be mainly directed towards the encouragement of a free action of the other excretories—the skin and bowels—and towards lowering the arterial blood-pressure. With these objects in view a hot air or steam bath should be given daily. Free perspiration may be assisted if necessary by means of frequent draughts of cold water. Some purgative also, calculated to produce copious watery evacuations, should be given in full doses; and for this purpose, either sulphate of magnesia or soda, or the compound powders of jalap, elaterium, or scammony, may be employed. The bowels should be kept loose by repeating the dose, if necessary, daily. Wet-cupping the loins to the extent of several ounces may be of service in cases in which the suppression is nearly complete, but the employment of dry-cupping, or the application of poultices to the loins, is practically useless. The hot air or steam bath is especially indicated when the skin acts badly, and when there is obvious anasarca; and in these cases a diaphoretic mixture containing acetate of ammonia, nitrate of potash, and spirits of nitrous ether may be given every three or four hours.

The diet should consist of milk only, preferably diluted with soda, lime, or barley water; and lemonade may be given freely. The vomiting may prove very troublesome, in which case the milk should be peptonised, and administered in small quantities. Though drugs are not usually of much service, the retching may sometimes be controlled by drop doses of tincture of iodine given hourly in a teaspoonful of water.

Most cases of scarlatinal nephritis will progress favourably under the above treatment. The re-establishment of the urinary secretion, attended by a fall in the blood-pressure, the disappearance of œdema, and a normal temperature, are the signs to be looked for. Under these circumstances, if the vomiting has ceased, the diet may be gradually extended so as to include bread and butter, farinaceous puddings, and white fish. Now is the time at which iron in some form is most useful, and none is better than the tincture of the perchloride given in 10-15 minim doses three or four times in the twenty-four hours.

When the case has so far progressed that no signs of nephritis remain (other than more or less albuminuria, and a certain degree of anæmia), the inclusion of a couple of boiled eggs in the dietary will be beneficial. This will tend to replace the albumin which is constantly being passed in the urine; and under the influence of an appreciable amount of coagulated proteid and the free exhibition of iron, a patient will usually put on flesh and gain colour with greater rapidity. If at any time uræmia threaten, as shown by drowsiness, headache, vomiting, and (more important still) the slightest suspicion of muscular twitching, the most energetic measures are called for at once. Then one or two drops of croton oil, floated in a teaspoonful of milk, should be given immediately; the body, well covered with blankets, should be at once placed in a hot air or steam bath, and $\frac{1}{6}$ to $\frac{1}{3}$ grain of pilocarpine injected subcutaneously. If the arterial tension be high, $\frac{1}{100}$ grain of nitroglycerine may be given; or better still, the patient should be bled, the amount of blood being regulated by the effect produced upon the pulse. The case must be carefully watched, and if the breathing become embarrassed, through spasm of the glottis or respiratory muscles, chloroform should be administered forthwith. A few whiffs will frequently relieve the respiratory spasm and consequent cyanosis. It should be repeated as many times as may be required. By its use not only is an immediate danger removed, but time is given for the other remedies to act. Many cases of uræmic convulsions have been saved by its judicious administration.

The onset of acute pulmonary œdema is, in my experience, invariably fatal. Venesection would appear to hold out the best prospect, and digitalis should always be tried with the object of contracting the pulmonary capillaries. During the acute stage of nephritis, and for a week or two afterwards, the patient should be kept between blankets, nor should he be allowed, under any circumstances, to get up for at least a month from the onset of the affection. He should in all cases be kept rigidly confined to bed until the amount of albumin has fallen to a trace, and flannel should be constantly worn next the skin, not only throughout convalescence, but for several months afterwards.

If the patient has been getting up for a week or two, gentle out-of-door exercise may be allowed in *dry* weather. This, if the body be warmly clad, will be of distinct benefit, even though a trace of albumin remain. A few weeks' change at the sea-side will in most cases complete recovery.

Persistent albuminuria, of more than three or four months' standing, probably always points to permanent impairment of at least some portion of the renal tissue. In these cases residence in a warm, dry climate, and extreme care in respect to both habits and diet, are indicated.

Eczema.—The treatment of this complication is for the most part comprised in the treatment of the condition which gave rise to it. An otorrhœa or rhinorrhœa should be dealt with in the manner already described, and means should be taken to prevent the child from picking the affected spots. The scabs should be removed by means of a small poultice, and either white precipitate or zinc ointment afterwards applied. The daily inunction of lanolin will prove serviceable in skins which are peeling after scarlet fever, especially during the winter months; and great care should be taken that children's skins should be thoroughly dried after washing. If the eczema be at all chronic, the exclusion of meat from the diet, and a course of arsenic, are indicated.

Ulcerative Stomatitis.—In mild cases nothing more is required than to syringe out the mouth every few hours with a solution of chlorine, Condy's fluid, or corrosive sublimate, and to paint the affected surface occasionally with glycerine of borax or nitrate of silver. The teeth should be kept carefully cleansed, and any carious stumps removed. In those severe cases which are known by the name of "Noma," the diseased and sloughing surface should without loss of time be scraped thoroughly with a curette, and fuming nitric acid afterwards freely applied. This operation may usually be done under cocaine, but in the worst class of case, or in those which have not come early under treatment, the disease may be so extensive that a general anæsthetic may be required. After operation the inside of the mouth should be brushed over with olive oil, and periodically syringed out with some antiseptic lotion. If after forty-eight hours the disease is seen to be extending at any point, the affected part should again be destroyed. Excision of the parts will rarely be required if the case be got under treatment sufficiently early.

Tonsillitis and Bronchitis.—The treatment of these affections presents no special feature, and should be conducted on ordinary lines.

F. Foord Caiger.

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F. F. C.

CHICKEN-POX

Synonyms.—*Varicella, Variola crystallina, Crystalli;* Ger. *Wasserpocken, Varicellen, Windpocken, etc.;* Fr. *Varicelle;* Ital. *Varicella.*

A specific infectious disease characterised by a vesicular eruption which usually appears in successive crops.

Chicken-pox was long confounded with small-pox, but since Heberden, in 1767, clearly distinguished the two diseases no authority of eminence, except Hebra, has affirmed their identity. The strongest facts in support of their non-identity are that neither chicken-pox and variola nor chicken-pox and vaccinia are mutually protective, and that chicken-pox breeds true. Several instances have come under my observation of vaccinated children between three and six years of age who suffered from chicken-pox, contracting small-pox after a short residence in a small-pox ward; and I have vaccinated with success numbers of unvaccinated children suffering from chicken-pox.

Chicken-pox arises solely from contagion, by direct contact with the sick, by the air for a short distance, by third persons handling the sick, or by means of infected articles. It is uncertain whether it can be inoculated or not; probably it is inoculable. In my experience it is a highly contagious disease—its infectivity being nearly, if not quite, equal to that of small-pox. It prevails occasionally in epidemic form, but is mostly endemic. Its highest seasonal prevalence is perhaps in autumn. Insusceptibility to its contagium is not uncommon, and one attack usually protects for life. Trousseau states that second attacks occur, and some German physicians have noted second and even third attacks. I have not seen a second attack. It is a disease of children mostly, both sexes being equally liable; the age of maximum incidence is from three to four years; but it often attacks infants, and may occur in adults. I have seen seven cases in persons over thirty; one of these was a woman aged seventy-one.

Incubation Period.—The older authorities believed this to be less than a week (four to six days), later observers said a week to fourteen days; but the most recent observations go to prove that it varies between the extremes of eleven and nineteen days, fourteen days being admittedly the most common. I have not seen it less than thirteen or longer than seventeen days. If inoculated, the incubation period is stated to be ten days. No facts have been recorded to prove whether chicken-pox may occur in utero or not; but Hubbard records a case of a baby that manifested chicken-pox the day after its birth, when the characteristic vesicles appeared, followed by a second crop on the next day. The mother was not suffering from chicken-pox, but her six other children were laid up with it. If the diagnosis was correct, either the child contracted it in utero, or the incubation period was one day.

Symptoms.—Children are often observed to be fretful for a few hours before the appearance of the eruption, and there may be slight rigors with rise of temperature to 99° or 100° F., with some loss of appetite and perhaps vomiting. On the other hand, there may be no initial symptoms. In rare cases the attack is ushered in by severe symptoms, such as delirium and convulsions; and Thomas records a case with a temperature of 106° F., and an initial general erythema. In hæmorrhagic cases there is slight rise of temperature; for two or three days before the eruption appears repeated hæmatemesis and hæmorrhage from the bowel may occur, followed by collapse and subnormal temperature; hæmorrhages may appear in the skin. In adults it is not unusual to find initial symptoms of headache, backache, slight rigors and malaise, lasting for one, two, three, or more days before the appearance of the eruption, and with or without a rise of temperature.

Eruption.—In children, when initial symptoms are absent, the presence of the eruption first attracts attention. It may all appear at once, and will then probably not be abundant. But in a very large majority of the cases successive crops appear from day to day, usually on not more than four, five, or six successive days, sometimes on as many as ten, with perhaps one or two days intermitted; the second and third crops are often more abundant than the first. It first appears almost invariably on the back, chest, and abdomen, but occasionally first on the face or limbs. It consists of small rose-coloured macules that fade when the skin is stretched: in outline they are irregularly circular or elongated, their shape not infrequently foreshadowing that of the subsequent vesicles. Occasionally they attain almost the size of blotches. In the course of a very short time—an hour or two usually—the macules are raised and hard—not, as a rule, the well-defined shotty hardness of small-pox papules, but a diffuse hardness; and many are faintly acuminated in the centre when the vesicle is just beginning to form. Some of the smaller papules, however, become hard and shotty. The rapidity of growth of the vesicles from macules that appear simultaneously varies very much. Some of the macules never emerge from the macular stage, but fade in the course of twenty-four hours; others become papules, subsiding after a day or two; while a few show minute vesiculation, and others become full-sized vesicles. After the appearance of successive crops the eruption is present in all its stages: macules, papules, clear shining vesicles, desiccating unruptured vesicles, and crusts. The vesicles, which are often smaller than the rose-coloured macules, arise as a rule in the central portion of the papules. They are almost invariably discrete. At the limit of their growth, which may be attained in from six hours to twenty-four or thirty-six, they are of circular or elongated dome shape, not depressed in the centre (or only in the very rarest instances), and filled by a serous fluid. They are transparent, shining, unilocular, and collapse if pricked and their contents pressed out. They are often encircled by a pink or red areola that disappears on pressure: it is often broad and irregular in outline, and is usually smaller on the face and extremities than on the trunk. If circular, the vesicles vary in size from that of a small pin's head to a split pea; if oval or elliptical, their long diameter measures three-sixteenths to three-eighths of an inch. When the vesicle ruptures, the whole of the fluid may escape and the walls collapse: if only a portion escape, the central part of the vesicle collapses more completely than the periphery; a minute crust forms in the centre at the point of rupture, and the vesicle then shows a central depression. Many of the vesicles get ruptured by scratching or other forcible means; but some large and many small ones desiccate unruptured, forming rounded, light to dark brown prominences of various sizes, not unlike the unruptured desiccating vesicles of modified small-pox. The areola gradually fades, and the crusts fall off in periods varying from five or six days to two or three weeks, exposing a reddened flat or slightly indented new epidermis on which some desquamation takes place.

On many ruptured vesicles, however, a flat or depressed, dark or even black crust forms; inflammation and ulceration take place underneath, often extending considerably beyond the original limits of the vesicle; pus oozes from the ulcerated surface, and an ecthymatous condition results. After a time—a week to ten days—this subsides, the ulceration heals, and there may remain a livid, indurated portion of skin showing a central scar. The induration and lividity gradually disappear, but the scar persists. Ulceration is more frequent in children than in adults, and on face and trunk than on limbs.

The fluid in some vesicles becomes faintly cloudy, but pus is not formed till after the rupture of the vesicle. Into some large vesicles a very small quantity of fluid only is exuded; these are raised, flat, and white in appearance, not unlike a small empty blister.

The vesicles on the hands and feet are almost invariably small, circular, hard, and shotty, contain a little fluid, only in the rarest instances show a central depression, and are indistinguishable from the vesicles of modified small-pox; those on the forearms and legs often have these characters, and, if the eruption be copious, some of those on the trunk likewise. The vesicles may not exceed a dozen, or there may be some hundreds. Often there are 50 to 100 or 200. I have seen an eruption so abundant as to be almost confluent on trunk and extremities.

The distribution of the eruption is, in the majority of cases, characteristic of the disease. It is most abundant on the trunk and sometimes also on the scalp; less abundant on the face, arms, and legs, and least of all on the hands and feet; the palms and soles being very often free from eruption. In a few rare exceptions to this rule it is found more abundantly on the face and arms than on the trunk. It also appears on the buccal mucous membrane, on the hard and soft palate, on the tongue, pharynx, and tonsils, on the vulva, and on the male genital organs. The character of the vesicular eruption varies as a rule with its distribution. Circular, oval, and elliptical vesicles are usually to be seen on the trunk, thighs, and arms; on the face and scalp, legs and forearms, they are mostly circular, and on the hands and feet almost invariably so.

The symptoms, even in later stages, are usually slight. The pyrexia is as a rule unimportant—the temperature in some cases not rising above normal during the course of the disease; in others it rises to 100° F., 102° F., or in rare cases to 103° or 104° F., simultaneously with or shortly after the appearance of each crop of eruption, falling to normal in the interval between them. The pulse is sometimes 90 to 100 or 110. During the first few days patients suffer little discomfort, except that caused by the often excessive itching of the eruption. The appetite is usually good, there is very little restlessness, and sleep is undisturbed. Painful micturition occurs owing to eruption on vulva. In hæmorrhagic and gangrenous chicken-pox the symptoms are severe, and the temperature may rise to 104° or higher.

Gangrenous Chicken-pox.—In this form multiple gangrene of the skin and subcutaneous tissue and the vesicles occurs, sometimes so deep as to expose the muscles. Pleurisy, secondary abscesses, and pyæmia may follow and death ensue. Such cases are usually observed in children already unhealthy and ill-nourished.

Hæmorrhagic Chicken-pox.—This form is very rare, and the vesicles are usually few in number. Large and small ecchymoses appear with hæmorrhage into the cutis under the vesicle, accompanied by hæmatemesis and melæna. The symptoms are severe, but recovery usually takes place.

Duration.—In cases uncomplicated by ulceration or gangrene, the acute stage lasts two or three days if there be only one crop of vesicles; three to seven, if several crops appear, and sometimes seven, ten, or twelve days. Convalescence is usually rapid. Infectivity lasts from the appearance of the eruption until the desquamation on the new epidermis has ceased. In many cases a fortnight suffices for this, but as some of the crusts adhere to the skin more tenaciously than others, the process is often not at an end until three or four weeks from the commencement of illness. The desquamation that follows after the healing of gangrenous surfaces is not to be regarded as contagious.

Complications and Sequels.—The epidermis remains reddened for a varying time, two to three or four weeks. Pitting often results after ulceration, and always if gangrene has occurred. Nephritis has been noted during the second week of disease. It usually terminates in recovery, but in syphilitic or unhealthy children it may prove fatal. Paraplegia, passing away on convalescence, has been noted in a rhachitic child a fortnight after the onset of the disease. I have seen one case complicated by pneumonia and another (an infant) by bronchitis, both fatal. Acute miliary tuberculosis has been known to ensue. Trousseau stated that he had seen a bullous eruption like pemphigus, lasting six or eight weeks, occur fifteen, twenty, thirty, or forty days after the commencement of the illness. Mr. Jonathan Hutchinson has recorded a number of cases that were followed by a persistent mixed papular and vesicular symmetrical eruption, avoiding flexures, prone to affect soles and palms, and very intractable.

Chicken-pox frequently coexists with whooping-cough, scarlet fever, measles, and diphtheria.

Diagnosis.—The differential diagnosis of chicken-pox and small-pox (for which disease it is most commonly mistaken) will be discussed in the article "Small-pox." Acne and vesicular and pustular syphilitic eruptions should not cause much difficulty. In molluscum contagiosum the small tumours are umbilicated and filled by a soft, white, granular substance that can be easily squeezed out. Small patches of herpes on abdomen and chest may look not unlike chicken-pox. By the aid of a lens the minute vesicles can be seen, and any doubt removed.

Anatomy.—The inflammatory process that takes place in the cells of the rete Malpighii only slightly affects the papillæ of the skin. The horny layer of the epidermis is raised up by the exudation of the serous fluid, and the vesicle is thereby formed.

Bacteriology.—Bareggi claims to have discovered an ovoid-shaped micrococcus in the white blood corpuscles on the fifth day of the disease, by inoculating cultures of which he has communicated chicken-pox to children. Guttman isolated a white and yellow staphylococcus, and a coccus which did not liquefy gelatine, and showed a yellow growth, but none of these are pathogenetic. Rille affirms that micro-organisms are less numerous in the suppurating vesicles than in the others, and Pfeiffer describes protozoa as present in the vesicular fluid (Guinon).

Treatment.—Mild cases do not require special treatment, but it is advisable that the patient be kept in bed for a short time, and light diet given. Hæmorrhagic and gangrenous cases require careful nursing, ample nourishment, and alcoholic stimulant if symptoms of collapse occur. If ulceration or gangrene set in, the patient must be kept in bed, and suitable antiseptic dressings applied.

JOHN MACCOMBIE.

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J. MacC.

SMALL-POX

Synonyms.—In Scotland still written *The Pocks* (pokes or pockets of matter); Arabian (Rhazes), *Jadarí;* Latin, *Variola* or *Variolæ;* French, *La petite Vérole;* Ital. *Vajuolo;* Span. *Viruelas;* Germ. *Blattern, Menschenpocken;* Danish, *Kopper;* Modern Greek, *Εὐλογία.*

Short Description.—An acute infectious disease, characterised by pyrexia and a general eruption of minute red macules, which in about eight days pass through the successive stages of papule, vesicle, and pustule.

History.—Small-pox dates from remote antiquity. The earliest knowledge of its occurrence is derived from India, where the Brahmins practised inoculation many centuries before the Christian era. In China it is said to have been known as early as 1100 or 1200 B.C., and inoculation was practised there in the end of the sixth century A.D. The date of its appearance in Western Asia is uncertain, and there is much difference of opinion whether small-pox was known to the ancient Greeks and Romans. Some believe the Plague of Athens, B.C. 425, to have been small-pox, and Eusebius gives an account of a disease very like small-pox that prevailed in Syria in 302 A.D. Not until the latter part of the sixth century, when it broke out in the Abyssinian army at the siege of Mecca A.D. 570, is definite information available as to its prevalence in Western Asia. In the tenth century Rhazes of Bagdad wrote his well-known treatise on *Small-pox and Measles*—the first medical work on small-pox. He quotes extracts from the works of Ahron, who practised in Alexandria in the seventh century, which show that small-pox was then a well-known disease in Egypt, and it had in all probability prevailed in Africa many centuries before that time.

Its introduction into Europe is ascribed by most authorities to the Arabs, who are said to have carried it with them at the beginning of the eighth century, when they conquered Spain, 710 A.D. It is certain, however, that it had invaded Europe and even Ireland before that date. According to Gregory of Tours, that state was desolated by it at the end of the sixth century, long before the Saracens invaded Spain, and it was prevalent at the same time in Italy. From the south it gradually spread to the north of Europe, and by the tenth century, if not before, it had reached Germany and the Low Countries. In Ireland it was known as early as the latter part of the seventh century, but it was not until the tenth century that it appears to have been recognised in England. The records of its endemic and epidemic occurrence in England during the Middle Ages are exceedingly scanty, but from indirect evidence it would appear to have prevailed widely in the fourteenth and fifteenth centuries.

The term small-pox (small pokkes) was first used in England to designate the disease in 1518, and had come into general use by the middle of the sixteenth century, when the disease was well known and widely spread throughout the country. In 1593 Kellwaye wrote the first English work on the subject (Creighton).

The London Bills of Mortality, first compiled in 1629, afford more precise knowledge of its occurrence, in London at any rate. From that year to the present time small-pox has been almost continuously present. In Scotland it was recognised in 1610. It was epidemic in Iceland during 1241 and 1242, and repeatedly thereafter; the most fatal outbreak being that of 1707, when 18,000, out of a population of 50,000, died. It prevailed in Sweden during the fifteenth century. It first appeared in the western hemisphere in 1507, when whole tribes in the West Indies were exterminated by it. Shortly after the discovery of America in 1492 it was introduced there, and its ravages were appalling. In South America it appeared in 1563 in Brazil.

In Great Britain during prevaccination times small-pox showed a periodic intensity of prevalence every three, four, or five years. Since vaccination was made compulsory in 1851, its periodic prevalence has varied widely in different towns and districts, but no really widespread epidemic has occurred except that of 1871.

In London there has been a greater incidence of small-pox since 1851 than in any other town in the kingdom. For instance, from 1851 to 1885 small-pox was continuously present; and there have been moderate epidemic outbursts every three or four years. But from 1886 to 1892 inclusive, in no year did the deaths exceed eleven; in 1889 there were no deaths from small-pox; in 1893, 1894, and 1895 there has been some prevalence of the disease.

Speaking generally, the longer duration of the inter-epidemic periods since 1851 depends upon a variety of causes, chief of which is vaccination; but the prompt isolation of small-pox patients, and, in London at least, the removal of all cases to hospitals several miles out of town, have doubtless been instrumental in limiting the spread of infection.

Susceptibility.—Of unvaccinated persons very few are insusceptible to the infection of small-pox; this insusceptibility has been variously estimated at from 1 to 5 per cent. Probably it is not more than 1 or 2 per cent; and most susceptible persons contract it on first exposure to infection. It attacks all races, but the negro is believed to be the most susceptible.

Small-pox is slightly more common among males than females, as the following table shows:—

Table showing Sex and Numbers of Small-pox Patients at Different Quinquenniads up to 29 years of age (Asylums Board Reports, London).

Ages.	Males.	Females.
Under 5 years	799	717
5 to 9 ,, ...	1,211	1,209
10 to 14 ,, ...	1,659	2,029
15 to 19 ,, ...	2,389	2,087
20 to 24 ,, ...	2,206	1,556
25 to 29 ,, ...	1,337	941
30 upwards	2,075	1,482
Total . .	11,676	10,021

At all ages, therefore, except in the quinquenniad ten to fourteen, the number of attacks is greater absolutely among males than females; and if due regard be had to the fact that after the first five years of life the number of females living is in excess of the number of males, the disproportion becoming greater in each succeeding quinquenniad, the greater incidence of small-pox in males is more apparent.

It is said that infants are not so susceptible to small-pox as children and adults, but this is doubtful. Of infants subjected to infection that have come under my observation, I have seen only one that failed to contract the disease, and that was a child born at the full time during the convalescence of the mother from an attack of discrete small-pox. There was no evidence that the child had had small-pox in utero. It was insusceptible not only to small-pox—so far as a month's residence in a ward full of small-pox patients without contracting the disease was evidence of its insusceptibility—but also to vaccinia. Infants, as a rule, are less exposed than children and adults not only to the infection of small-pox, but to that of other infectious diseases.

Pregnancy and childbirth do not appear to increase the susceptibility to small-pox, nor do persons suffering from or convalescent from other acute infectious diseases appear to be more susceptible to small-pox than those in ordinary health. On the contrary, there is some reason to believe that, in the acute stage at least, they are less susceptible to it than are healthy persons.

In countries where small-pox had been widely prevalent for generations, it was, prior to the introduction of vaccination, a disease mainly of children, as are scarlet fever, measles, hooping-cough, and diphtheria at the present day; nearly all individuals contracted it in infancy or early childhood, and the majority of the survivors were thereby protected against it for life. But when it attacks an unvaccinated population for the first time, or after a long period of immunity, all ages are affected alike.

Small-pox has at one time or another prevailed in every quarter of the globe, with the exception of Australia, where, although introduced on several occasions by emigrants, its spread has been promptly checked by the isolation of the sick.

Climate and Season.—Climate appears to influence its prevalence in some degree, this being greater in tropical countries than in cold; in warm climates its prevalence is favoured by cold and retarded by heat, and in tropical countries the rainy season is said to check the disease.

The season of the year affects its prevalence, but not in a very marked degree. In temperate climates, at all events, summer is the season of least, and spring, autumn, and winter the seasons of greatest prevalency. I have frequently noticed that in outbreaks commencing in autumn there has been a sudden drop in June of the following year, and that the lessened incidence prevailed during the summer months. It is not probable that this drop is due only to the more airy habits of life in summer.

Contagiousness.—Boerhaave, in the beginning of the eighteenth century, was the first to prove that small pox was spread by contagion exclusively, although its contagious nature had for a long time been known. The fact of the Brahmins and Chinese having practised inoculation renders it probable that they recognised this feature of the disease. The Arabs were familiar with it, and it was known in England as early as the fourteenth century. The contagion may be either direct or indirect, and it has lately been shown that the virus may be carried from a small-pox hospital, by the air, a considerable distance, without losing its infectivity. The virus enters the human body by the mucous membrane of the nose, mouth, or respiratory tract; some believe also by the mucous membrane of the stomach. One observer in this country (Birdwood) believes it to be received through the skin. It may be communicated from the sick to the healthy by—(*a*) Persons suffering from small-pox; (*b*) Bodies of persons who have died of small-pox; (*c*) Infected articles; (*d*) Healthy third persons; (*e*) By the air to persons living at some distance (aerial infection); (*f*) Inoculation.

(*a*) Small-pox patients are capable of communicating infection to others, perhaps during the stage of incubation, certainly during the initial stage, and right through the disease till not a trace is left on the skin of desiccated pustules or scabs, or of the subsequent desquamation. But the infection is much more virulent at certain stages of the disease than in others; it is most virulent during vesiculation, pustulation, and scabbing, less so during the initial stage and the first and second days of rash, and least of all during the incubation stage. The distance at which a single patient may communicate infection to a healthy person varies from the closest contact to a few yards, much depending upon the ventilation of the apartment. As a rule a susceptible person will be infected merely by entering the room or ward occupied by the patient. The severity of an attack of small-pox appears to be determined more by the personal susceptibility of the recipient of the contagion than by the severity of the disease in the person imparting it. Even the mildest form of modified small-pox in one person may cause pure hæmorrhagic small-pox in another, and *vice versa*.

(*b*) The bodies of the small-pox dead are capable of communicating infection, but probably only to those who handle them.

(*c*) Infected articles such as bedding, wearing apparel, books, toys, coins, furniture, rags, or anything handled by patients, are capable of communicating infection. Infected rags have frequently given rise to outbreaks of small-pox.

(*d*) Healthy third persons in attendance on patients may communicate infection to others, either by means of their clothing or by the hair which readily retains the particles of dried small-pox matter which permeate the air of an infected room.

(*e*) It may be conveyed directly by the atmosphere from a small-pox hospital to persons living at some distance. How far is a point on which there is great difference of opinion. Mr. Power, in his investigations at the Fulham Small-pox Hospital, showed that the incidence of small-pox bore a very exact relation to propinquity to the hospital. The incidence on every 100 houses within the special area (a radius of a mile from the hospital) was as follows:—On total area, 6·37. On small circle (one quarter mile), 17·35. On first ring (quarter to half mile), 9·25. On second ring (half to three-quarter mile), 6·16. On third ring (three-quarter to one mile), 2·57. The influence was greatest when admissions to hospital were beginning to increase. The comparison held good with regard to successive epidemics, and he did not regard the hospital administration as responsible. Dr. Barry showed that a similar incidence of small-pox around the hospital prevailed at Sheffield during the epidemic of 1887-1888; and confirmatory evidence of a like character has been obtained from other localities. It is now pretty generally admitted that Mr. Power's conclusions hold good as regards small-pox hospitals, but Dr. T. D. Savill, in a report on a small-pox outbreak at Warrington in 1892-1893, came to the conclusion that the diffusion of small-pox by aerial currents (from the hospital) was not an appreciable factor in the Warrington epidemic.

(*f*) Inoculation is not practised in civilised countries; it is illegal, and has only a historical interest.

Incubation Period.—When a person receives the specific infection of small-pox there is in most cases a definite interval between that time and the onset of the earliest symptoms, during which no apparent deviation from normal health is noted. This interval varies in different individuals: in a few exceptional cases symptoms of malaise occur from the date of reception of infection. It varies between extremes of five days and twenty or more; usually it is twelve days, but not infrequently ten, eleven, thirteen, or sometimes nine. Curschmann records a case in which it was only five; I have seen it as short as seven; and Armstrong (*Lancet*, vol. i. 1886, p. 715) has given particulars of a case in which it appeared to be twenty-one days. Some foreign observers have noted it to be twenty,

twenty-two, and twenty-three days, but such lengthened incubation periods, as well as the extremely short, are very exceptional.

Initial Symptoms.—The onset as a rule is sudden, and the early or initial symptoms are usually distinctive of the disease. The most constant symptom is headache,—frontal, occipital, or over the entire head, but most commonly frontal. It is often intense, in many cases throbbing, in others lancinating in character; it is aggravated by movements. Backache is the next most constant symptom, and is, of all the initial symptoms of small-pox, the most characteristic; headache being frequently met with in the early stages of other acute infectious diseases. The backache is lumbar and sacral, and is usually severe, in many cases excruciatingly so; the pain may extend from the sacrum down the thighs and legs. Both headache and backache last till the eruption comes out, or for some little time after. Rigors, severe or slight, are often present with the other initial symptoms. Epigastric pain accompanied by vomiting is also an early and, especially in children, a very usual symptom. The vomiting and retching are sometimes excessive, the patient being unable to retain even the smallest quantity of nourishment. Anorexia and thirst are present in every case. The fauces do not as a rule present any abnormal appearance in the initial stage; the tonsils may be enlarged, and in hæmorrhagic cases purple hæmorrhages may be noticed on the soft palate. I have not seen diphtheria present. The breath is often fœtid and the tongue coated with a white or dirty white fur; the skin is usually hot, dry at first, but afterwards moist or even sweaty. Pallor is often marked, and may be accompanied by coldness of the extremities; but in many cases there is flushing of the head and face, accompanied by visible pulsation of the carotids. Constipation occurs in nearly all cases. In children drowsiness is often present, and sometimes tremors and twitchings accompanied by grinding of the teeth during sleep. The drowsiness may pass into coma which may be preceded by convulsions. In adults coma is rare. Delirium is sometimes present on the second or third day, and is occasionally marked; but is usually only slight. Most patients are sleepless and restless. Vertigo is by no means rare. Paraplegia has been noticed, and also retention of urine. Prostration often accompanies the other symptoms, and the patient usually takes to bed or sits over the fire. In females at or above the age of puberty menstruation often occurs before the usual menstrual period; in many cases more than the usual quantity of blood is lost, and in hæmorrhagic cases the amount may be large or even excessive. The urine is diminished in quantity, its specific gravity is increased, and it usually contains urates in abundance; albumin may be present, but rarely in large quantity. There may be blood in the urine, but this occurs infrequently, and mostly in cases that afterwards prove to be hæmorrhagic. The temperature, except in some hæmorrhagic cases, is high from the onset of the initial symptoms. At first it is 100° to 101° F., and may reach 104° F. on the first day; on the second day it may be as high as 105° or 107° F. It remains raised, with very slight morning remissions, until the eruption comes out. The pulse is rapid, often 110 to 120 or more in adults, and in children 150 or more. In most cases it is full, fairly strong, and regular; but in cases accompanied by much depression it is weak and rapid. In pure hæmorrhagic cases it is soft, compressible, and sometimes dicrotic; such patients not infrequently experience a sensation of cardiac and respiratory oppression. The respiration is quick and short, and when coma is present it may be stertorous. There is no perceptible enlargement of liver and spleen, nor tenderness on pressure over these organs.

The initial symptoms (headache, backache, and pyrexia) last till the eruption begins to appear, in many cases until it is fully out; and they often subside as suddenly as they appeared. The epigastric pain and vomiting are usually most marked early in the initial stage; but sometimes, especially in hæmorrhagic cases, vomiting may last until the termination of the disease. The *average duration* of the initial stage is two days, but it may not be more than one, or it may be three or more. In some cases the initial symptoms are gradual in onset, mild in character, and may be of short duration; in such cases the attack usually proves mild, but the converse does not hold good: patients whose symptoms in the initial stage are exceedingly severe, or who are convulsed or comatose, may pass through mild attacks, but most cases of severe small-pox are ushered in by severe initial symptoms.

Initial Rashes.—Along with the initial symptoms just enumerated a series of eruptions may appear on the skin, which, from their occurrence in the initial stage of the disease, are known as initial rashes. These may be divided into two great groups—(1) the Erythematous, and (2) the Hæmorrhagic.

1. *Erythematous Rashes.*—These may be either (*a*) general or (*b*) partial in distribution.

(*a*) *General Erythemas.*—These are usually scarlatiniform or morbilliform in appearance. In many cases they do not cover the entire surface of the skin, limited areas being free from eruption. They usually cover the trunk, limbs, and, to a less extent, the face and neck. They may appear on the first day of illness, more generally on the second, sometimes on the third, fourth, or even fifth day. They persist for a period varying from two to five days, disappearing in some instances before the characteristic eruption of small-pox appears, in other cases simultaneously with its appearance, and in others not until one, two, or three days after the small-pox eruption is out. They reach their height in from twenty-four to forty-eight hours, and often disappear completely twelve hours thereafter, and leave no stain. In other cases they disappear more slowly.

The scarlatiniform erythema resembles the eruption of scarlet fever, but it is usually less punctate and not of so bright a scarlet colour; in the groins and flexor surfaces of joints is often of a deeper tint than elsewhere. It is not raised; it disappears on pressure, and is not accompanied by faucial inflammation or enlargement of the cervical or submaxillary glands. But occasionally an intensely vivid rash is seen, which appears sometimes on the first, more frequently on the second day of illness, covers the entire surface of the skin, and is of a uniform brilliant red colour, closely resembling the blush of erysipelas. This has been called by some an erysipelatoid initial rash. It disappears on pressure, is often the precursor of grave hæmorrhagic symptoms, and lasts a varying period; in hæmorrhagic cases it may last till death; in other cases until the second or third day after the appearance of the characteristic eruption of small-pox, when it fades gradually and leaves no discoloration of the skin.

The morbilliform erythema is of the pink colour of measles, is very slightly, if at all, raised, disappears on pressure, and shows in parts the crescentic appearance often noticed in measles. It usually reaches its height within twenty-four hours of its first appearance, and fades quickly either just before the characteristic eruption of small-pox appears, or soon after, leaving no stain. The maculæ are from the first larger than the minute maculæ of the early stage of measles eruption. The rash spreads over the whole body more quickly than that of measles, and in the great majority of instances is not preceded or accompanied by catarrh, sneezing, or cough; not infrequently, however, there is considerable suffusion of the eyes.

(*b*) *Partial Erythemas.*—These are usually scarlatiniform or morbilliform in appearance, and affect the flexor or extensor surfaces of joints and circumscribed areas of other parts of the skin. If limited to flexor surfaces they are distributed on the lower part of the abdomen, the inner surfaces of the thighs, and the flexor surfaces of the joints of the extremities, palms of hands, and insteps of feet. In other cases they are limited to flexor surfaces of limbs, or to the inguinal region, armpits, sides of trunk, and lumbar region. In others they are only seen on the extensor surfaces of the extremities; where they are limited to the back of the hands, the wrists, or above the wrists, the elbows, knees, and dorsum of foot, and the extensor surface of the great toe, between its inner border and the tendon of the extensor longus hallucis. They appear from the first to the fourth day of the disease, and, if morbilliform, are very slightly if at all raised above the surface of the surrounding skin; they fade sometimes before the eruption of small-pox appears, more frequently shortly after; but if they appear simultaneously with the characteristic eruption of small-pox they do not fade until after the lapse of from two to four days. They disappear on pressure and no staining results. The partial erythemas appear to vary a good deal in character and distribution in different outbreaks; but they are invariably followed by mild attacks.

2. *Hæmorrhagic Rashes.*—These are of two kinds—(1) Petechial, (2) Petechio-erythematous. They appear on the first, second, or third day of illness, are not attended by itching, but sometimes by a sensation of heat in the skin of the affected part, are not raised, and usually precede, but sometimes appear simultaneously with the characteristic eruption of small-pox.

(1) *Petechial Rashes.*—These are most frequently observed on the lower

abdominal and inguinal regions—on an irregularly shaped triangular area, the base of which is formed by an imaginary horizontal line across the abdomen, sometimes at, sometimes above, sometimes below the umbilicus, the apex being in mid-line between the thighs four to five inches below the pubes. The sides of the triangle run outwards and upwards from its apex, parallel to and three or four inches below Poupart's ligament, to the great trochanter, and thence upwards to meet the base line. This is by far the most frequent site; but in some cases the rash extends on the lumbar region, and, in a more scattered form, up the sides of the chest; sometimes it is present in the axillæ, sometimes on the neck, and on the chest under the clavicles; in others on the flexor surfaces of the joints. The rashes vary in colour with the varying proportions of the different petechiæ present, which are of two colours, bright brick red and dark purple. The bright red petechiæ are small, round or irregular in outline, vary in diameter from a point to a line, are rather deeper in colour at the centres than at the edges, and fade slightly, but do not disappear on pressure. The purple petechiæ show, if seen when making their appearance, as minute purple dots which speedily increase in size till they are one to two lines across, and are round or irregular in outline with ill-defined margins. The two kinds of petechiæ are usually present together, imparting to the affected area a purple hue tinged with red. As the rash increases the purple tint becomes deeper, and the red petechiæ begin to fade. If the purple petechiæ be very thickly set at first, they coalesce and form large areas of a deep purple hue. In the abdomino-crural triangle abovementioned the purple petechiæ are usually most abundant along and just above and below Poupart's ligament, where they impart to the skin a deep purple, almost black colour; while the skin towards the margins of the triangular space remains of a mixed purple and red hue.

In some cases the bright red petechiæ only are present, and may cover the skin of the abdomen and lower part of chest, the flanks and lumbar region, or they may be limited to the groins and flexor surfaces of the joints of the extremities. If extremely abundant in these situations they impart to the skin the appearance of being covered by a punctate scarlet rash; but on pressure their petechial character is apparent by the fact that while fading slightly they do not disappear. In other instances the purple petechiæ only are present, and, as a rule, eruptions composed of these are less widely distributed than those composed exclusively of the bright red petechiæ.

There is another form of initial rash, not very often met with, that is indistinguishable both in distribution and in appearance from ordinary purpura, and therefore may be named "purpuric initial" to distinguish it from the "petechial initial." It consists of circular purpuric spots two to four lines in diameter, of the colour of ink or of the deepest violet, with well-defined margins and regular in outline. This eruption does not show a preference for the flexor or extensor surfaces or the abdomino-crural triangle, but is distributed irregularly over the trunk and limbs, and is unaccompanied by any other initial rash. It occurs usually in children, invariably precedes the characteristic eruption of small-pox, is not accompanied by hæmorrhage from the mucous surfaces or elsewhere, and the spots are limited in number.

(2) *Petechio-erythematous Rashes.*—These are formed, as the name implies, by a combination of petechial and erythematous eruptions. The erythema may be general, but is more often partial, and frequently limited to the abdomino-crural triangle, sides of trunk, lumbar region, axillæ, neck, and flexor surfaces of limbs. It usually covers a larger area than the petechial portion of the rash.

When at its height the petechio-erythematous rash, if situated in the abdomino-crural triangle, presents a red, sometimes a deep red colour at the borders, deepening in colour towards the more central portions, where it often assumes a deep purple, almost black colour. The petechiæ are usually much more closely set at the central portions than at the borders. The skin is in most cases smooth, but in some it is faintly raised and rough, owing to the appearance of a few minute vesicles. Should the patient recover, the erythema disappears in a few days, but the petechiæ, especially the purple ones, fade slowly, leaving a brownish discoloration which, gradually changing to yellow, ultimately disappears completely.

The petechial and petechio-erythematous rashes reach their full development in about two or three days, are usually not raised and do not itch. If they are accompanied by hæmatemesis, hæmoptysis, hæmorrhages from the mucous surfaces and kidneys, and in women by metrorrhagia, they almost invariably foreshadow hæmorrhagic small-pox. The lighter the colour of the petechial portion of the eruption the greater is the probability of the attack ending in recovery, and conversely.

The Eruption.—The characteristic eruption of small-pox appears, as a rule, forty-eight hours after the onset of the initial symptoms; but there are many exceptions to this rule. In some cases a solitary papule appears on the face, hand, or elsewhere on the first day of illness, and is not followed by others until the usual time. In other cases numerous papules appear on the second day followed by an abundant eruption on the third day, and occasionally the eruption does not appear until the fourth day of illness. The earliest papules are usually found on the face, arms, and back of wrists and hands, and are soon succeeded by others on the lower extremities and on the trunk. In a number of cases they appear on all parts of the skin simultaneously; in others first on the inner surfaces of the thighs, or on the nates. Simultaneously with its appearance on the skin, the eruption appears on the buccal mucous membrane, the tongue, hard and soft palate, fauces and pharynx; also on the vulva, sometimes on the vagina, and on the lower part of the rectum. The eruption does not extend down the œsophagus, but is often present in the larynx, and occasionally in the trachea as far as the bifurcation or a little lower. Sometimes a vesicle forms on the conjunctiva, but never on the cornea.

The eruption is not distributed uniformly; as a rule it is most abundant on the face, scalp, extremities and back, whilst the skin on the front of the chest is less affected, and the skin of the abdomen least. Generally speaking, it is less abundant on the flexor surfaces of elbows and knees, and in axillæ and groins, than on the extensor surfaces. Where petechial or petechio-erythematous rashes appear, there is usually little, if any, characteristic small-pox eruption. In natural small-pox it varies in amount from a few hundred vesicles to thousands; and if it be discrete the vesicles may sometimes be noted in groups of twos, threes, and fives. In cases modified by vaccination the whole of the eruption, in most instances, is out within twelve hours from the appearance of the first papule; but in natural small-pox, especially in confluent cases, the papules continue to appear until the third day of the eruption. It may frequently be noted that the eruption is more copious on areas of skin subjected to special pressure than elsewhere; for instance, round the waist in women, on the skin of the leg under the garter, on the shoulders of men under the braces, and also on areas where a local irritant has been applied before the appearance of the eruption, round varicose sores, etc.

Up to the appearance of the characteristic eruption the course of the disease and the symptoms are alike in natural small-pox, and in small-pox modified by vaccination; but at this stage so wide a divergence in the course of the natural and of the modified diseases begins, that it is desirable that the symptoms of each class should be described separately. I shall therefore review in detail the course of the eruption and the symptoms that are typical of natural small-pox, and thereafter describe the course of modified small-pox, reserving the varieties of small-pox—(1) small-pox without eruption, (2) discrete, (3) confluent, and (4) hæmorrhagic—for later description.

NATURAL SMALL-POX.—The eruption of natural small-pox consists at first of minute bright red macules which disappear on pressure, and are neither hard nor raised. In the course of a few hours they increase in size, and are distinctly hard, red, and raised. The macule has now become a papule, and the stages of its growth from a papule to a vesicle, from vesicle to pustule, and its desiccation, are as follows:—In the course of twenty-four hours the papule has swelled visibly, and shows at its apex a small vesicle commencing to form, which grows slowly but steadily. Day by day it widens at its periphery, at the same time filling out with serum, till at the fifth day of eruption it has attained the limit of its growth. It is surrounded by a thin red line or areola from its commencement. A full-sized vesicle is about one-fifth of an inch across, circular, well raised above the level of the skin, translucent, of the colour of dull pearl, with rounded border, in many cases showing a central depression, and its base encircled by a narrow but distinct zone of redness. It is filled with clear, transparent serum; on being pricked a small quantity of this exudes, but the vesicle does not empty, nor do its walls collapse. The central depression, or, as it is often termed, the umbilication of the vesicle, is invariably to be noted in a large number of vesicles, but not by any means in all. Between the fifth and sixth days of eruption a minute central opaque dot is visible on its surface; this opacity enlarges towards the periphery day by day. As the opacity increases the vesicle swells, loses at the same time its central depression, and acquires by degrees a hemispherical shape; the surrounding areola becomes brighter, and in three, or at most four, days from the period of full vesicular growth—that is to say, on the eighth or ninth day of eruption—it presents a circular, dome-shaped appearance, is completely opaque, is surrounded by a vivid areola, and has now become a pustule. On running a pin through it from side to side pus or turbid lymph escapes, and on forcibly emptying the pustule its walls collapse.

The papules of natural small-pox are red, raised, and hard. If the finger be firmly pressed on the skin and drawn slowly across it, the papules feel like small shot embedded in the skin. These characteristics last till the papule has attained some degree of vesiculation, and all through the vesicular stage the vesicles are hard and resistant.

The areola is present from the earliest stage of the vesicle, and is at its height on the eighth to the ninth day of eruption. It is brightest at its inner margin, shading off towards its periphery, is raised, and in the pustular stage is often more or less indurated. It begins to fade with the bursting and desiccation of the pustules.

The pustule, if it be not ruptured forcibly, remains intact for a day or more, when it ruptures, usually in the centre; pus escapes, and, rapidly drying, forms a dirty yellow crust.

From the first appearance of the macule the successive stages of papule, vesicle, and pustule with incrustation occupy about ten or eleven days. The crusts now begin to fall off, exposing a red surface, that may be raised, flat, or depressed; in the last case it may or may not be ulcerated; or the crusts may adhere for a week or more unless removed by suitable applications. Many of the pustules do not rupture, but their contents, by partial absorption or evaporation, become inspissated and of a brownish colour. The walls shrivel, and the pustule losing its dome shape becomes flattened; after a time its walls rupture, and the dried contents and epidermis fall off together, exposing in some cases a raised, in others a flat, and sometimes a depressed, red, new epidermis.

Concurrently with the development of the eruption on the skin, the vesicles on the lips, tongue, palate, tonsils, and pharynx increase in size and present a round, more or less flattened, white appearance. Even at the limit of their growth, which they attain sooner than the vesicles on the skin, they are smaller than those on the latter situation, and only sometimes are surrounded by an areola. The mucous membrane swells, and about the fifth day of eruption many of the vesicles rupture, exposing a ragged, ulcerated surface; this, if the eruption be confluent on the fauces and palate, has the appearance of dirty disintegrating diphtheritic membrane. The shreds of mucous membrane come away, the ulceration heals, the swelling of the parts subsides, and the throat resumes its normal condition about the time the crusts are falling off the skin.

Such is the course of the ordinary small-pox papule through the several stages of macule, papule, vesicle, pustule, and incrustation. It must not be imagined, however, that all the vesicles on a patient's skin attain their full development simultaneously. Those that appear first maintain their lead throughout; and those on the face are, in point of development, usually a day in advance of those on the lower extremities: but on any given part of the body some vesicles are in advance of others, and later, while some of the pustules have ruptured and crusts are forming, some shrivel and abort, others desiccate unruptured. So that on the limbs, for instance, there can usually be seen dirty yellow scabs and brown, desiccated, unruptured pustules mixed together. On the face, however, most of the pustules burst. When the crusts have fallen off, and the ulceration healed, a branny or powdery desquamation follows not only on the part of the skin covered by the pustule, but on the inner margin of the skin affected by the areola. If the pustules desiccate, unruptured desquamation often takes place on the areolar surface, sometimes before, sometimes after the desiccated pustule has separated from the skin. The desquamation is then usually branny rather than powdery.

Symptoms.—In some cases simultaneously with the appearance of the characteristic eruption, in others not until it be fully out (second to third day of eruption), there is an abatement or complete cessation of the headache, backache, and many of the other initial symptoms; and the patient is, but for the itching and discomfort due to the eruption, usually free from pain or restlessness, and expresses himself as being fairly comfortable.

The temperature, which at the height of the initial symptoms may have reached a height of 104° F. or higher, begins to fall soon after the eruption appears; and by the end of the first or on the second or third day of eruption it has fallen in discrete cases to 99° F., or even to normal: but in confluent cases it often does not fall much below 100° F. This remission continues in mild cases till the vesicles begin to show opacity, but in severe cases the period is shorter. The temperature now rises with the process of pustulation till, when the pustule is mature, it reaches a height in discrete cases of 102° F., and in confluent cases of 104° F. or higher. This is the so-called secondary fever of small-pox. The morning remissions are usually one or two degrees. Along with the processes of desiccation and incrustation the temperature falls, till at about the tenth to the twelfth day in uncomplicated discrete cases—eleventh to the thirteenth in favourable confluent cases—it is normal. The duration of the rise of temperature depends, in uncomplicated cases, on the depth of ulceration of the skin and the amount of concomitant dermatitis.

In the early stage of eruption, with the fall of temperature, the pulse slows to 80 or 90; in mild cases even to the normal; in confluent cases to 90 or 100: it remains slow till the pustular stage, then it becomes rapid, and in discrete cases is usually full and regular; but in confluent attacks at the height of the pustular stage it becomes very rapid—120 to 130 or more, and visible pulsation of the carotids may often be noticed. In the pustular stage the first sound of the heart is often blurred and indistinct, and the pulse weak, irregular, and sometimes dicrotic.

The frequency of respiration corresponds with the rapidity of the pulse; but in confluent cases the breathing is often shallow, laboured, and stertorous in the height of the pustular stage: if laryngitis accompanied by much dyspnœa occur, the lower ribs and sternum fall in.

With the growth of the vesicles the skin begins to swell, most noticeably on the face, neck and limbs. At or before the height of the vesicular, and in the pustular stage, there is much subcutaneous œdema; the eyelids are often intensely swollen, and can only be opened with difficulty, if at all. In confluent cases the nose is twice its normal size, the scalp and ears are swelled, the lips enormously so, the mouth stands open, and saliva trickles from it in a constant stream; the cheeks and neck are baggy, the contour lines of face, chin, and neck are obliterated, and the features so disfigured that the patient is not recognisable by his nearest friends. The extremities — the forearms, hands and feet especially—are œdematous and painful, the fingers being kept in a partially flexed position, while the weight of the bed-clothes and the pressure of the mattress on the skin cause much suffering and discomfort. With the progress of the incrustation process the swelling of the skin subsides, and the patient's features begin to resume their normal appearance, though blurred in many cases by the presence of scabs which fall off slowly, and by dirty powdery débris and desquamation.

The dermatitis in mild cases is very slight if any; but in many of the confluent cases it is well marked. The areola changes to a fiery red colour, becomes indurated in proportion to the amount of inflammation, the crusts adhere tenaciously to the cutis, and when they fall off a more or less deeply ulcerated surface is exposed.

Thirst continues throughout the disease, but is much increased in the pustular stage, and in severe cases is excessive. Salivation is a very common symptom in confluent cases. The mouth cannot be closed, partly on account of the swollen condition of the mucous membrane, and partly on account of the swollen state of the lips and face generally. Sordes collect on the teeth and gums, the tongue is dry, the fauces and pharynx, already swelled and covered by mucus and shreds of disintegrated mucous membrane, become dry and parched. The breath is foul, and there is often much fœtor. There is usually little or no vomiting or sickness, liquid nourishment being taken freely and retained. Constipation is the rule during the whole course of the disease, but diarrhœa occurs in the pustular and scabbing stages in a certain proportion of severe cases, and in some mild cases.

Some degree of laryngitis with tracheitis and bronchitis, accompanied by cough and expectoration, are present in all severe cases from an early stage; the cough is often husky and laryngeal, and accompanied by stridor. Conjunctivitis, with some muco-purulent discharge, is present in many confluent cases.

The urine is secreted freely in the vesicular stage, and usually also in the pustular. In the latter the quantity of urea is largely increased, and in confluent cases albumin is present in about one-third of the cases, sometimes in large amount. Hæmaturia is rare except in hæmorrhagic and pustular hæmorrhagic cases. Retention of urine is exceedingly rare.

In mild cases the mind is clear, but in severe attacks confused delirium is frequently present. The delirium of small-pox varies much in character according to the stages of the disease in which it occurs. In the vesicular stage it is often noisy, violent, and crafty; in the pustular stage less noisy, sometimes violent, but more often of the muttering character. In discrete cases it is usually absent both in the vesicular and pustular stages; but in many confluent and vesicular hæmorrhagic cases it is often exceedingly troublesome during the vesicular stage, and requires most careful watching.

Emaciation is not a feature of mild small-pox, but in severe cases, complicated by extensive dermatitis, cellulitis, deep abscesses, and serious lung mischief, it is considerable and may be extreme.

If the course of natural small-pox, unattended by hæmorrhagic symptoms, be towards recovery, the symptoms present in the pustular stage subside simultaneously with the progress of the incrustation of the pustules, and the patient becomes rapidly or gradually convalescent according to the mildness or severity of the attack. But in unfavourable cases the severity of the symptoms increases, the temperature rises sometimes to 107° F., and the patient dies usually between the twelfth and sixteenth days of illness. In other cases the symptoms of the pustular stage subside, and death occurs later from lung or other complications. Death may be due to hypostatic congestion of the lungs, to catarrhal pneumonia, sometimes, but rarely, to lobar pneumonia, to dermatitis and consequent interference with function of the skin, to septicæmia, occasionally to pyæmia, and in aged persons with fatty hearts to cardiac syncope.

MODIFIED SMALL-POX.—A large proportion of the cases that occur nowadays in a well-vaccinated community are of the modified form. In many instances so completely is the course of the eruption altered and the symptoms, after the initial stage is over, are so modified that it is often difficult to recognise the identity of the ordinary and the modified diseases.

In modified small-pox, as a rule, the whole of the eruption is out within twelve hours of the appearance of the first papule. In ordinary cases it is not abundant, and may be macular at first or from the very beginning papular. In either case much of the eruption is usually vesicular within twelve to twenty-four hours, and the vesicles attain their full growth in about three days, while some of the papules abort without becoming vesicles. In size they are usually smaller than those of the natural small-pox, less regularly circular, more conical, and very often not depressed in the centre, although many show a faint line of redness from the beginning. On the third and fourth days of eruption the vesicles are opaque, the lymph is cloudy, and in many patients they do not become pustules, but desiccate unruptured, the inspissated lymph forming small, brown, flat and slightly-raised prominences about the size of a small sago grain or less under the epidermis. If they do become pustules they attain the stage of full pustulation within five or six days of the appearance of the eruption, and thereafter desiccate, ruptured or unruptured as the case may be. The crust or desiccated pustule falls off in the course of a week or less, exposing a flat, reddened, healed surface of epidermis, where usually a little desquamation follows.

Within a few hours of the appearance of the eruption the symptoms of the initial stage vanish, and the temperature falls to normal; in some cases it may rise again a degree or two, but in many it remains normal throughout the subsequent course of the disease: the constitutional symptoms are accordingly of the mildest description. There is little restlessness, the mind may, in severe cases, be confused, but delirium is usually absent, and thirst, if present, is moderate. The intense irritation, amounting in many cases to torture, often to be noted in those suffering from confluent attacks of natural small-pox, is completely absent. The appetite is good, and the patient complains of little but the discomfort arising from the vesicles and pustules, which may render the skin tender to touch and pressure. In a week or little more, often less, the patient is well; and by the end of a fortnight or less from the beginning of his illness he is up and about. Dermatitis, salivation, and fœtor are absent. There is little if any swelling of the skin of the extremities; but not infrequently, if the eruption be fairly abundant, the face, especially the nose and eyelids, is swelled, and the lids œdematous; in most cases the features are quite recognisable throughout the disease. No complications of importance arise, unless it be a few boils, or an occasional attack of facial erysipelas, slight conjunctivitis, or an occasional corneal ulcer. The appetite is good, and patients take nourishment well from the time that the eruption appears on the skin. Recovery is rapid and complete, and patients can with difficulty be restrained from going into public before they are free from infection.

These are the symptoms and course of modified small-pox; but it is well to remember that many cases are much milder than is indicated in the above description, while some may be more severe, though death rarely results. If it do occur, it is usually due to accident or intercurrent disease.

I have described natural and modified small-pox without special reference to the character and amount of eruption, or the severity of the symptoms. For descriptive purposes, however, it is desirable to regard these features of the disease, and to divide small-pox into four classes, which include nearly all the cases met with in actual practice—(1) **Small-pox without eruption**; (2) **The discrete small-pox**; (3) **The confluent small-pox**; (4) **The hæmorrhagic small-pox**—and to consider separately in each class the natural and the modified forms, bearing in mind that natural small-pox is not restricted to unvaccinated persons, but may occur in vaccinated subjects in whom the immunity afforded by vaccination from an attack of small-pox has ceased.

Premising that the incubation period, initial stage, and date of appearance of eruption are alike in the four classes, I now proceed to a detailed description of each.

1. Small-pox without Eruption.—Occasionally such cases are seen. The initial symptoms are those already described, and may be either mild or severe, or may be accompanied by a partial initial erythema. At the time that the characteristic eruption usually appears the symptoms subside, the temperature falls to normal, no eruption appears, and the patient, after an interval of a day or two, is quite well. I have only seen such cases in vaccinated, and sometimes in revaccinated subjects; one such case apparently communicated the disease to another person who passed through an attack of modified small-pox.

2. Discrete Small-pox.—A. *Discrete Natural Small-pox.*—The full amount of eruption is out usually within twenty-four hours of the appearance of the first spot; on the fifth day of eruption (seventh of disease) the vesicles are full size, encircled by a narrow areola; on the seventh to the eighth day of the disease a central opaque dot is seen in many of the vesicles, and by the ninth day most of them are quite opaque, and those on the face are pustular, a bright areola encircling each. The pustules on the face rupture first, and small, light or dirty yellow crusts form. On the extremities and trunk some rupture, others desiccate unruptured, and towards the end of the second week of the disease in many cases the scabs are falling off and the patient is convalescent. The temperature usually falls to normal in the vesicular stage, rises a few degrees in the pustular, but is seldom higher than 101° to 102° F., and falls with the desiccation of the pustules. The pulse is seldom over 100. There is a good deal of swelling of the face and skin generally; and during the late vesicular and pustular stages the patient suffers pain and much discomfort from the eruption, and in addition there may be sore throat due to eruption on the fauces. The mind is sometimes confused, but delirium is very rare. In children under two or three years of age, and especially in infants, the dermatitis may be considerable. The condition of the fauces in infants interferes with swallowing, and they take nourishment with difficulty. Lung complications are rare except in infants and children up to four years of age, in whom laryngitis, bronchitis, or catarrhal pneumonia may occur. Dermatitis, multiple superficial abscesses, erysipelas, cellulitis, transient facial paralysis, conjunctivitis or corneal ulcer, and otitis occur as complications, but mostly in young children, convalescence in those over five years of age being usually uninterrupted. Deep pitting occasionally results, but usually not, and there is often none at all. Death may be due in infants and children to dermatitis, to cellulitis, or to laryngeal and lung complications; and in adults to lung complications during later stages.

B. *Discrete Modified Small-pox.*—If the eruption be fairly copious the distribution is that described under natural small-pox. It is not abundant as a rule, and the number of vesicles may not exceed half-a-dozen; usually there are a few vesicles on face, limbs, and trunk; but I have seen a case with only five vesicles all told, and these situated on the nape of the neck. Much of the eruption is vesicular within twelve to twenty-four hours of its appearance, but in some rare cases the papular stage lasts for a couple of days before this happens. The course of the disease is short; the temperature falls to normal with the appearance of the eruption, and in very many cases does not rise again. In the mildest attacks the patient feels quite well after the initial symptoms have subsided, and the disease, so far as regards subjective symptoms, is at an end.

In more severe cases the temperature rises to 99° or 100° F. during the pustular stage; the pulse is slightly accelerated, but the constitutional symptoms are very slight, and the patient is convalescent within a week or eight days of the onset of the disease. It is free from danger to life, and convalescence, save for an occasional boil or rare attack of facial erysipelas, is usually uninterrupted.

Rare Forms of Discrete Small-pox, attended by severe Nervous Symptoms.—Some attacks of discrete small-pox in vaccinated and unvaccinated subjects are ushered in by great mental disturbance, delirium, convulsions, and perhaps coma. In some cases these symptoms subside at the usual period; but in others there is no intermission of the initial delirium, which becomes more and more violent, and merges into acute mania that may last several weeks. The symptoms may gradually abate, and the attack result in complete recovery; but in others permanent dementia may result. In other cases the coma of the initial stage gets more profound, and the patient dies in a few days without regaining consciousness. In a few instances convulsions set in about the seventh to the ninth day of illness, coma rapidly supervenes, and the patient dies in twenty-four to forty-eight hours. Only in very rare cases does recovery take place. The symptoms are usually due to congestion of the brain, and sometimes to hæmorrhage under the pia mater. The temperature usually rises to 105° or 106° F. before death.

In a few very rare cases of small-pox symptoms of great mental confusion, with loss of the power of co-ordination, occur in the initial stage, accompanied by aphasia and sometimes by partial or complete paralysis of the extremities. This state lasts a varying time, one, two, or three weeks, when the patient begins to recover the use of his limbs, and the power of articulation returns slowly, the utterance being difficult, thick and jerky. The paralysis and loss of co-ordination last a very long time after the patient is convalescent, and the walk of the patient in many respects resembles that of tabes dorsalis. Time, however, brings gradual improvement, the general health is good, and the symptoms ameliorate if complete recovery do not take place.

3. Confluent Small-pox. — A. *Confluent Natural Small-pox.* — This includes all degrees of confluence, limited in some to small areas of confluent vesicles in face and extremities; in others the skin of face, neck, limbs, chest, and back is completely covered by vesicles. In the former the eruption is fully out within twenty-four to thirty-six hours of appearance of the rash, in the latter not until the second or third day of eruption. Shortly after the appearance of the eruption, the skin of the forearms and face often becomes deeply hyperæmic, in some cases uniformly erythematous; and as the vesicles grow, their paler outlines are thrown into relief against the reddened background of skin. The temperature falls in milder cases to 99° F., or to normal, but in the severer not much, if at all, below 100° F. During the period of vesicular growth in milder cases the patient is free from restlessness, and but for the itching and discomfort of the eruption feels tolerably well; in severer cases, especially those in which the eruption is completely confluent on the face and extremities, there is intense irritation and discomfort towards the end of the vesicular period. So acute is it that patients often tear the epidermis completely off the arms, legs, and face, exposing a raw surface, from which a sero-sanguineous fluid exudes. The skin dries rapidly, becomes stiff, rough, and of a deep mahogany colour. In these cases the temperature does not fall below 100° F.; extensive dermatitis ensues, the temperature rises to 104°-105° F., or higher; there is extreme restlessness, much delirium, rapid pulse, and the patient succumbs about the ninth to the eleventh day of the disease.

In the majority of confluent cases, as the vesicles approach their full growth, there is considerable subcutaneous œdema, most marked on the face, neck, forearms, hands and feet. At the height of the vesicular period, and in the pustular stage, the eyelids are often intensely œdematous, the upper eyelid overlapping the lower; the patient is quite unable to open his eyes, and the lids can with difficulty be separated. The nose, cheeks, and lips swell enormously, the neck even in a greater degree; the hands and feet are swelled and acutely tender to the touch, the fingers being partially flexed. There is copious eruption on the buccal mucous membrane, fauces and pharynx; saliva trickles incessantly from the open mouth. A day or two later pus oozes from freshly-ruptured pustules, and from under the freshly-formed scabs, and the patient presents a picture of hideous disfigurement and helpless bodily discomfort without a parallel in acute infectious diseases. There is high temperature (103° to 105° F., or even higher), quick pulse, rapid breathing, cough, and expectoration of mucus, foul mouth, much fœtor, unquenchable thirst, extreme restlessness, sleeplessness, and often delirium. Dermatitis follows, sometimes moderate in degree, but often coextensive with the eruption. In favourable cases, coincidently with the incrustation process, the subcutaneous œdema subsides, the eyes open, and the scabs fall off; the features begin to resume their normal outlines, and the patient about the beginning of the third week of the disease generally enters on the stage of convalescence. In unfavourable cases, and these form 50 per cent of the confluent attacks, the temperature in the pustular stage rises to 105°-107° F., the pulse becomes rapid, weak and irregular; there is husky, laryngeal cough, rapid, shallow breathing sometimes attended by dyspnœa, much fœtor, muscular tremors, and sometimes diarrhœa; the urine and fæces are passed involuntarily, delirium is more or less constant, merging into semicoma, and the patient succumbs usually from the tenth to the fifteenth day of the disease. If the patient survive till decrustation be well advanced, pleurisy, pneumonia—in children usually catarrhal pneumonia—deep and extensive cellulitis, diarrhœa or other complication may supervene; and such complications often prove fatal.

One striking form of confluent small-pox deserves separate notice. In some of the completely confluent cases the vesicles at the usual period of full vesicular development (fifth to sixth day of eruption) are flat, with shallow central depression, only partially filled with serum not translucent, but of a dirty white hue; there is not much, if any, subcutaneous œdema; the features though blurred are recognisable; the eyelids are not œdematous; there is little swelling of the face, hands, or feet other than that due to the raised vesicles; the skin is rough and flat, presenting the appearance of coarse parchment. The temperature in the vesicular stage ranges from about 100° to 102° F.; the pulse is rapid and weak, the mind is confused; there is great prostration, but not usually much discomfort; there is no conjunctivitis, but a non-inflammatory keratitis often occurs, the first sign of which is a dulness of the cornea rapidly changing to cloudiness and complete opacity. The whole cornea may become opaque in twenty-four to thirty-six hours from the onset of the keratitis; a portion or the whole of it may slough off in a day or two, and partial or complete anterior staphyloma result. The keratitis sometimes affects both eyes, but usually only one, or one less extensively than the other. This form of confluent small-pox is usually fatal, death taking place from the ninth to the eleventh day of the disease. Occasionally recovery takes place in patients between ten and twenty years of age, but it is slow and protracted, and there is much emaciation.

B. *Confluent Modified Small-pox.*—The course of cases of this class is precisely similar to that of confluent natural small-pox till about the third or fourth day of the eruption, when the vesicles have attained their full growth, being in most instances considerably smaller than those of confluent natural small-pox. There is often great swelling of face and neck, and pronounced œdema of the eyelids, as well as subcutaneous œdema of the extremities; the temperature may rise to 100°, 102°, 103° F. for a day or two. But at this time a remarkable change in the course of the eruption takes place. Instead of the vesicles continuing to grow till the fifth day of the eruption, they show on the third or fourth day a central opacity, or become uniformly cloudy, and by the fifth day are completely opaque; a few may become pustular, but the great majority shrink, become brown, and desiccate unruptured, the skin being thickly studded with innumerable raised brown specks, about a line in diameter, more or less. At the same time the subcutaneous œdema subsides, the temperature falls, and the patient about the eighth or tenth day of disease, when natural small-pox is just at its height, enters on convalescence, which in most cases is uninterrupted except by the occurrence of boils. The vesicular, pustular, and desiccative stages are all shortened.

4. Hæmorrhagic Small-pox.—This includes cases in which cutaneous and subcutaneous hæmorrhages appear with or without the presence of the characteristic eruption of small-pox on the skin. It is convenient for descriptive purposes to divide these into two groups: the *first* including those cases characterised by the presence of numerous cutaneous and subcutaneous hæmorrhages, by bleeding from the mucous surfaces and kidneys, and by a complete or all but complete absence of the characteristic small-pox eruption, which are known as hæmorrhagic or black small-pox; the *second* including those cases exhibiting, in addition to the characteristic eruption of small-pox, cutaneous and subcutaneous hæmorrhages, accompanied or not by bleeding from the mucous surfaces and kidneys, which are known as vesicular or pustular hæmorrhagic small-pox.

(1) *The Hæmorrhagic or Black Small-pox.*—This is by no means rare. It occurs both during epidemic and non-epidemic periods. The majority of attacks occur in vaccinated persons. The initial symptoms are almost invariably severe, especially the backache; and there is often violent and long-continued vomiting, attended by severe epigastric pain. The temperature in the initial stage is not high, usually not above 100° F., often below it. Very early in the course of the disease the cutaneous and subcutaneous hæmorrhages begin; they are of three kinds—the brick-red petechiæ, the purple petechiæ, and the violet or ink spots described under the heading of initial rashes. These cutaneous hæmorrhages may or may not be preceded or accompanied by either general or partial erythemas, which appear usually on the first or second day of the illness. The general erythema is often of a vivid red colour; the partial erythemas are of the character described under initial rashes. On the second or third day red and purple petechiæ may appear in masses in the groins, the flexures of joints and elsewhere, with violet or ink spots a little later, to be succeeded by subconjunctival hæmorrhage in one or both eyes, usually beginning in the inner aspect of the eye, and gradually extending round till, if the patient live long enough, the cornea is encircled by a deep purple band of ecchymosis. Purple spots appear on the forehead and face; minute purple petechiæ appear on the eyelids, gradually increasing in size and number until the eyelids assume a blue-black appearance. Bruise-like patches, varying in size and situation, and suggestive but independent of contusion, not infrequently appear. Purple hæmorrhages may often be seen on the tongue, palate, and fauces, but the mucous membrane is generally pale. Blood oozes from the gums, in rare instances from the skin, and epistaxis, hæmatemesis, hæmoptysis, and melæna may occur. Blood is passed in the urine, and in women from the vagina and uterus. The masses of hæmorrhage in the abdomino-crural triangle and other flexures get darker, and the violet spots increase in number. The temperature is usually low, seldom over 100° F.; often normal or even subnormal. The pulse is soft and compressible; the mind absolutely clear and unclouded. The breath is clammy, but there is not much fœtor if any.

Nourishment is taken fairly. The patient is restless, and often complains of a sense of oppression in the præcordium. The backache is most severe and persistent. Retinal hæmorrhages sometimes occur, and may cause partial or total blindness.

As the disease progresses, sordes collect on the gums; the skin of the face, dotted by purple and ink spots, becomes of an ashy hue, and perhaps a little puffy; the lips and tongue are blanched. In some cases, perhaps, half-a-dozen papules may be seen on close examination on the back of the hands, on the dorsum of the foot, or on the forehead or cheeks; but in other cases not a single papule. In the great majority of cases the mind is unclouded to the last. Death may take place as early as the third, more often on the fourth, fifth or sixth day, and is frequently due to sudden cardiac syncope.

In some cases no erythema is present, and there may be but a small number of large violet ink spots on the trunk and extremities, and a few smaller purple petechiæ, accompanied by epistaxis, hæmatemesis, and blood in the urine.

An exceedingly rare and rapidly fatal form of the black small-pox has been described in which the initial symptoms are most severe: the temperature reaches 105° or over, with delirium, coma and collapse, rapidly terminating in death after an illness lasting a few hours. No skin hæmorrhages are seen, but internal hæmorrhages similar to those described on p. 227 are found. I have not myself seen this fulminant variety.

Black small-pox rarely occurs in vaccinated subjects under the age of puberty. I have not seen it in those under seven years of age. Young, vigorous and apparently strong and healthy adults, are not infrequently attacked by it. I have not met with a case in any one who had one-third of a square inch of well-foveated vaccination cicatrix, and who had been successfully revaccinated. Recovery does not take place from this kind of small-pox.

(2) *Vesicular and Pustular Hæmorrhagic Small-pox.*—This class includes a very large number of cases occurring among vaccinated and unvaccinated subjects. There are two varieties. A. Cases which, in addition to hæmorrhagic symptoms of varying intensity, show a considerable amount of characteristic small-pox eruption. B. Cases in which the hæmorrhage is confined to the cutis under the vesicle and into the skin immediately surrounding the vesicle, with or without hæmorrhages from the mucous membranes. These may be named sub- and peri-vesicular hæmorrhagic cases.

A. Hæmorrhagic cases attended by more or less abundant characteristic small-pox eruption.

Generally speaking, in this class a fairly copious eruption of vesicles succeeds the hæmorrhagic appearances and symptoms, and the amount of characteristic eruption is usually in the inverse ratio to the severity of the hæmorrhagic symptoms; not only do hæmorrhages take place into skin free from eruption, but there is often hæmorrhage into the cutis under the vesicle, and into the skin immediately surrounding the vesicle. The temperature in these cases is usually above 100° F., and if the patient live till the pustulation begins it rises to 103°-104° F. The mind is always more or less confused, and there is often active and violent delirium, the degree of mental confusion and delirium being usually in direct ratio to the amount of characteristic small-pox eruption. The face and limbs swell in proportion to the amount of the small-pox eruption. The pulse is rapid, weak, and may be irregular. Respiration is quickened and shallow, cough is usually troublesome. Sordes collect on the gums. There is usually much eruption in fauces, while dried mucus adheres to the mouth and throat, and blocks the nostrils, and thirst is excessive. There is often much fœtor. In fact the symptoms approach those of confluent natural small-pox.

With very rare exceptions indeed, patients affected with this kind of small-pox do not recover. The duration of life is longer than in the pure hæmorrhagic cases, and shorter than in the natural confluent cases; it is directly proportioned to the amount of small-pox eruption present, and in inverse ratio to the amount of skin and other hæmorrhages. Death usually takes place from seventh to tenth day of disease.

B. Sub- and peri-vesicular hæmorrhagic cases.

In these cases there is an absence of ordinary cutaneous and subcutaneous hæmorrhages. The small-pox eruption may be discrete or confluent; the papules and line of redness round the vesicles are, however, often of a deep angry red, or even purplish colour. The vesicles develop in the usual way, but about the third day of the eruption a dark central discoloration appears in the vesicle; it quickly enlarges, and, in twenty-four hours or less, the vesicle has a uniform purple or leaden appearance; simultaneously with this change, if not before it, there appears round the base of the vesicle a claret-coloured areola, about a line in width, which does not fade on pressure. These sub- and peri-vesicular hæmorrhages may be coextensive with the eruption. They are often seen on the lower extremities, especially on the legs; in other cases on the lower and upper limbs and trunk, and in others on the face also. As the vesicles fill and are distended by serum, which is usually quite clear and free of blood or hæmoglobin, the subvesicular hæmorrhages disappear from view, but the clarety areolæ persist. There is usually hæmorrhage from the mucous surfaces, and sometimes from the kidneys, but this is not so marked as in the other variety of hæmorrhagic cases (Class A). There is often much fœtor, great thirst, and usually delirium. The temperature ranges between 99° and 102° F. in the vesicular stage; and in the pustular rises to 103°-104° F., or even higher. The pulse is rapid and weak. Recovery is not infrequent, especially if sub- and peri-vesicular hæmorrhages be confined to the lower extremities, and to a few vesicles on trunk or arms; but if the hæmorrhage be on the face, trunk and extremities, and the eruption confluent, recovery does not take place. I have seen a fatal case of discrete small-pox, with sub-vesicular hæmorrhage under every vesicle, but no purple spots or petechiæ, and not a trace of hæmorrhage from mucous surfaces. Vesicular and pustular hæmorrhagic small-pox may be either confluent or discrete, but is most commonly confluent, and attacks both vaccinated and unvaccinated subjects.

Pseudo-hæmorrhagic Cases.—There is a form of small-pox sometimes called hæmorrhagic vesicular, in which the appearances are as follows:—No cutaneous or subcutaneous hæmorrhages penetrate either into the parts of the skin free from eruption or into the skin under the vesicles. About the fourth or fifth day, when the vesicles are filling with serum, they acquire a purple colour, tinged with red, due to the vesicular fluid being stained by hæmoglobin. The vesicle is usually well filled, and on being pricked reddish serum escapes. This is a totally different condition from the sub-vesicular hæmorrhage above described, which appears on the second to the fourth day of eruption, and disappears from view as the vesicle fills with clear lymph. It is usually met with in vaccinated subjects, and is very often seen on the lower extremities. In women some uterine hæmorrhage may occur. These pseudo-hæmorrhagic cases usually recover, and are not infrequently recorded as recoveries from black small-pox.

Anomalous Forms of Eruption.—During the pustular stage, in some discrete cases, in vaccinated or unvaccinated subjects, the epidermis of the skin at the base of the pustule is raised by an exudation of clear or straw-coloured fluid. A bulla like a pemphigus blister is formed with the pustule anchored or floating in the centre.

In certain cases of modified small-pox some of the vesicles on the face, especially on the nose and cheeks, do not desiccate and fall off in the usual manner. The lymph appears to become partially organised, and a verrucose condition results.

Owing to the modifications produced in the characteristic eruption by vaccination, many forms of small-pox based on these modifications have been described, such as miliary, crystalline, acneiform, and so forth; but the varieties are fanciful rather than important.

Mr. Marson described a variety based on the distribution and aggregation of the vesicles, which he named corymbose small-pox. Clusters of vesicles like corymbs appear at different parts of the skin, and the attacks were usually if not invariably fatal. This variety I have not seen.

Inoculated Small-pox.—On the second day after inoculation the skin at the points of inoculation is puckered, and of a yellow colour. On the third day a papule has formed; on the fourth a vesicle. On the sixth day, if inoculation has taken place in the arm, the axillary glands are swelled and painful, and on the seventh or eighth day the vesicle has become a pustule. The temperature is raised, and there may be headache, backache, and vomiting, followed soon—eighth to tenth day—by the characteristic general eruption of small-pox. Inoculated small-pox usually but not invariably ran a mild course.

Second Attacks.—These are very rare. Many small-pox patients state that they have had a previous attack, but if careful inquiry be made into the symptoms, distribution of eruption, and duration of illness, and if the scars, if any, be examined, the alleged first attack will usually turn out to have been chicken-pox. In three-fourths of the cases of alleged second attack that have come under my notice, I was able to satisfy myself that the first attack had been one of chicken-pox; and in most of the others there was not sufficient evidence to show whether the first attack had been small-pox or not. I have not seen an attack of small-pox in any person who bore unmistakable evidence of having had small-pox. Second attacks usually run a mild course like that of modified small-pox, but severe second attacks are said to have occurred. I have seen a mild attack of small-pox forty years after successful inoculation.

Small-pox after Revaccination.—Such cases occur, but in the majority of cases it will be found that the revaccination had been unsuccessful. Some persons who have been successfully revaccinated do, however, contract small-pox. Of such cases observed by me the time intervening between the revaccination and the attack of small-pox varied from one to twenty-five years; the average being ten years. The attack is usually mild and modified, but I have seen a case of pure hæmorrhagic small-pox in a woman who stated that she had been successfully vaccinated four years previously; and on her arm were scars alleged to be due to and indistinguishable from those resulting from vaccination. I have not, however, seen fatal small-pox in any one whose primary vaccination was efficient, and who had also been successfully revaccinated.

Small-pox in the Fœtus.—This is said to have occurred as early as the fourth month. The liability of the fœtus to small-pox is not great, but it appears to increase directly with its age. It is, however, exceptional to find that the children born of variolous mothers, even during convalescence, have had small-pox in utero, or that they are suffering from it at the time of birth. There is some reason to believe, indeed, that they are more or less protected against small-pox by the mother's attack. Of half-a-dozen infants born of variolous mothers which have come under my observation only one had small-pox at the time of birth. But infants have been born at the full time who had evidently passed through an attack of small-pox in utero. Cases have been recorded of infants showing the eruption of small-pox well developed at birth, the mothers not having had small-pox; and in one such case the mother is said to have contracted small-pox from her infant.

Complications.—*Skin and Subcutaneous Tissues.*—Multiple abscesses are the most frequent of all complications. They appear during or after the completion of the process of scabbing, are situated usually on the extremities or the scalp, are superficial, vary in size from that of a large pea to a walnut, or larger, are unattended by much pain or constitutional disturbance, and are often present in large numbers. Large abscesses on shoulders, hips, limbs and neck are not uncommon. Ischio-rectal abscess occurs occasionally. Pressure abscesses and bed-sores rarely occur. Gangrene of the toes is even more rare.

Erysipelas is not infrequent; it comes on during the scabbing stage or later, mostly attacks the face and scalp, or the arms, and sometimes the scrotum; it is apt to spread, and is attended by pyrexia. When extensive, the constitutional symptoms may be severe, and the patient, if weakened by a severe attack of small-pox, is not unlikely to succumb.

Deep cellulitis, usually affecting the extremities, supervenes in some confluent cases during the late pustular or scabbing stage. It is often extensive, sometimes involving a whole limb; the affected part is red, brawny, and hot to the touch; pyrexia is high, constitutional symptoms severe, and it often proves fatal.

Obstinate acne pustulosa of the nose and face is not uncommon during convalescence.

Eyes.—Conjunctivitis is present in a large proportion of confluent, and in a small proportion of discrete cases. In adults it is not often severe; it occurs mostly during the vesicular and pustular stages, but sometimes during convalescence. In unvaccinated infants and children under three years of age it is not infrequently severe, and may be attended by palpebral dermatitis, with hard swelling of the lids, the upper so overlapping the lower that it is with the utmost difficulty that they can be opened. In favourable cases it subsides with the commencement of convalescence, but occasionally non-inflammatory keratitis sets in; the cornea becomes rapidly opaque, and sloughs, with the formation of partial or complete anterior staphyloma. Phlyctenular ulcers of the conjunctiva are not uncommon. Corneal ulcer is common, rarely affects both eyes, is usually superficial, and is attended by photophobia, lachrymation, and injection of the corneal zone of vessels.

Acute inflammatory keratitis occurs in some severe cases during the pustular or incrustation stage. Photophobia and increased intra-ocular tension are usually present; usually the inflammation is often limited to one-half of the cornea, is sometimes accompanied by hypopyon, in other cases by sloughing, and formation of a deep perforating ulcer. It usually affects one eye, or if both eyes, one less severely than the other. If the ulcer be not very deep, the opacity often disappears in time, though it is sometimes permanent.

Non-inflammatory keratitis occurs during the late vesicular or pustular stages, and is most frequently noticed in very confluent cases, especially those in which the vesicles are flat, and give to the skin the appearance of parchment. There is complete absence of injection of vessels of the conjunctiva, or of the corneal zone; and no photophobia or lachrymation. The first sign of its onset is diminished lustre of the cornea, which looks dull and sluggish: it quickly becomes cloudy, and the whole cornea may become opaque in from twenty-four to thirty-six hours. In a day or two it sloughs, discharge of the aqueous follows with prolapse of the iris, protrusion of the lens, and complete anterior staphyloma; or even panophthalmitis may ensue. In other cases only a portion of the cornea may slough, and if the perforation be small, a small staphyloma only result. This form of keratitis is often limited to one eye, but if both be affected, one usually less than the other. Blindness due to small-pox is usually a result of this non-inflammatory keratitis.

A peculiar form of corneal ulceration is sometimes met with. It is quite superficial, begins at the margin of the cornea, gradually creeps from one side to the other, and denudes the cornea of its epithelial layer. It is accompanied by pain, photophobia, and injection of the corneal zone of vessels and of the conjunctiva; infiltration of the deeper layers of the cornea does not occur. As the ulceration progresses the renewal of the epithelium follows on closely, the ulceration showing as a thin line as it creeps from one side of the cornea to the other.

Retinal hæmorrhage occurs in some hæmorrhagic cases, and the patient complains of being unable to see with one of his eyes. Iritis and cyclitis are very rare. Orbital cellulitis occurs in a few cases.

Otitis is not common, but, if it occur, it is usually otitis media of one or both ears, and may end in partial or complete deafness. It appears sometimes in discrete, but usually in severe cases and during the pustular stage. Mastoid abscess is very rare.

Respiratory Tract and Lungs.—Nasal catarrh is rare, and only occurs in a very few confluent cases. Epistaxis is not uncommon in hæmorrhagic small-pox. Laryngitis is usually caused by the presence of vesicles on the mucous membrane of the larynx: it occurs in vesicular or pustular stages in a large number of confluent cases, and occasionally in discrete. Its onset is usually gradual, and is attended by husky voice, laryngeal cough, and not infrequently by dyspnœa which may render tracheotomy necessary. Immediate relief is often thereby obtained, but unless the patient be young, and the attack of small-pox not very severe, recovery seldom takes place. Most confluent cases that present symptoms of laryngeal obstruction have much bronchitis and often hypostatic or catarrhal pneumonia in addition. Laryngitis occasionally occurs during convalescence. Perichondritis with necrosis of cartilages occurs in a few cases. Œdema of the glottis is rare. Bronchitis is universal in severe cases, and is attended by frequent cough and much expectoration. Catarrhal pneumonia is exceedingly common in confluent cases, and in vesicular and pustular hæmorrhagic small-pox. In unvaccinated children it is a frequent cause of death. Lobar pneumonia is fairly common, and usually occurs in pustular and incrustation stages; sometimes during the stage of decrustation or during convalescence, and for the most part in confluent cases. Pleurisy with suppurative effusion is also fairly common in severe cases during the incrustation and decrustation stages. Gangrene of lungs and œdema of lungs are very rare. Collapse of portions of lungs is not infrequent in laryngeal cases. Congestion of lungs is present in most cases of severe confluent and in all varieties of hæmorrhagic small-pox.

Digestive System.—Glossitis is of rare occurrence, and occurs in the vesicular or pustular stages of confluent cases, rarely in discrete cases.

It is attended by much pain; the tongue is often enormously swelled, fills up the cavity of the mouth, protrudes from the lips, and prevents the patient from taking nourishment. It is usually a fatal complication. Parotitis is occasionally seen.

Ulceration of the palate, fauces, and pharynx, attended by a ragged condition of the mucous membrane due to rupture of the vesicles, is not infrequent; and if the eruption be very copious, the fauces and tonsils appear to be invested with dirty white diphtheritic membrane; but the condition only resembles, and is not diphtheria. Diphtheria is very rare indeed in small-pox. Ulcerative stomatitis occurs, but gangrenous stomatitis I have never seen.

Heart.—Pericarditis occurs, but very rarely. Ulcerative endocarditis is extremely rare. Myocarditis occurs in a large number of the confluent cases.

Abdominal Viscera.—Peritonitis occurs in rare cases. I have seen extensive peritonitis in two cases after abortion, once (extensively) in an adult male along with pleurisy, once limited to the left hypochondrium and to the epigastrium in a patient whose spleen was studded by large emboli. Albuminuria occurs in about one-third of the confluent cases. Nephritis is exceedingly rare, but may follow during convalescence. Cystitis occurs occasionally.

Nervous System.—(*a*) Acute stage. The intense headache of the initial stage is not infrequently attended by delirium, in some cases by convulsions or coma. In the vast majority of instances these nervous symptoms subside or disappear entirely on the appearance of the eruption; but in a number of confluent cases, especially those of the vesicular hæmorrhagic type, although there may be some diminution of the delirium after the eruption has appeared, the lull is but temporary, and it soon becomes noisy and violent, and lasts until shortly before the death of the patient. Hallucinations, delusions, and melancholia occur, but usually disappear after a short time. Anæsthesia and hyperæsthesia, with or without paralysis, are of occasional occurrence. (*b*) Desiccation stage and convalescence. Facial paralysis occurs in a few cases, and always terminates in complete recovery. Peripheral neuritis is rare. Myelitis with paraplegia, paralysis of the bladder, occurs sometimes in the late pustular stage, and I have met with it during convalescence; but it is a rare complication. Westphal describes a case of paraplegia, in which he found small foci of softening widely distributed in the gray and white substance of the cord.

The symptoms of insular sclerosis, tabes dorsalis, and acute ascending paralysis proving fatal in a few days with no recognisable lesion, have been known to follow small-pox. Cerebral hæmorrhage occurs chiefly in vesicular or pustular hæmorrhagic cases. Its onset is quite sudden, and if the hæmorrhage be extensive, recovery does not take place.

Pyæmia occurs in a few, and is sometimes accompanied by acute disorganisation of some or all of the principal joints. Septicæmia occurs in some cases, attended by deep ulceration of the skin, and in those with extensive and deep cellulitis.

Rheumatism is exceedingly rare, but may occur in convalescence. *Phlebitis*, usually of the lower limbs, may happen during the incrustation stage or later. *Orchitis*, often double, with effusion into tunica vaginalis, is not infrequent, usually in the pustular and incrustation periods. *Ovaritis* occurs occasionally. *Paraphimosis* is sometimes seen in children.

Pregnancy.—Liability to abortion increases directly with the age of the fœtus and the severity of the attack of small-pox. In hæmorrhagic and confluent cases abortion invariably occurs if the patient survive long enough—sometimes in the initial stage, more frequently later. It is usually attended with considerable hæmorrhage, and in some cases the placenta is retained and has to be detached. In discrete small-pox abortion may, but more often does not, occur.

Sequels.—*Pitting.*—In cases in which there has been little if any ulceration of the skin the pitting is slight or none. At first, on the separation of the desiccated scab, there is in many cases considerable hypertrophy of skin at the site of the pustule, the epidermis being reddened and raised. In course of time this subsides and leaves the skin quite smooth or faintly pitted. But in cases in which there is deep ulceration of skin the pitting is marked and sometimes excessive, being most noticeable on the face. The extent and depth of pitting are in direct ratio to the extent of the inflammation of the papillæ of the skin and the consequent ulceration.

A *verrucose* or warty condition of the skin of the nose and cheeks results not infrequently from deep ulceration. In a few confluent cases in which there is deep ulceration and much dermatitis, bands of cicatricial tissue form, and a *cheloid* condition results. The face, which is the part usually affected, becomes scarred and disfigured; ectropion and distortion of the mouth may result.

Alopecia is noticeable only after severe attacks, and is usually more marked in adults than in children. If the ulceration of the cutis of the scalp be so deep and extensive as to destroy the hair follicles, permanent partial, sometimes almost complete alopecia follows. But in many cases the hair grows again in great abundance.

Pigmentation.—When the desiccated scabs fall off there is in all cases a red discoloration which lasts a considerable time. In vesicular and pustular hæmorrhagic cases there is dark pigmentation of skin, usually most marked on the lower extremities. This pigmentation lasts a long time and disappears very slowly.

Post-febrile insanity is a rare sequel of small-pox, and usually ends in complete recovery.

Tuberculosis of the lungs occasionally follows a severe attack of small-pox either during convalescence or later.

Convalescence lasts a varying period—from a week in the mildest case to many months in the most severe; a few patients never completely regain their health. But in most cases ultimate recovery is complete, and it is not an unusual occurrence to hear patients assert long after recovery from severe small-pox that they enjoy better health than before. Recovery from discrete, and mild confluent small-pox unaccompanied by hæmorrhagic symptoms, whether in vaccinated or unvaccinated subjects, is in almost every case rapid and complete. Many vaccinated patients are well from the time of the appearance of the characteristic eruption. Recovery after severe confluent, and vesicular and pustular hæmorrhagic attacks, whether discrete or confluent, is usually slow, and may be retarded by the occurrence of serious complications.

The **duration of the infectious period** is so variable that a hard and fast rule as to its limits cannot be laid down. It varies from a week in the mildest to two months or more in very severe cases. In ordinary discrete cases it lasts usually three to four weeks. A patient is not to be regarded as free from infection till all the crusts and desiccated pustules have fallen off, and the subsequent desquamation on and around the newly-formed epidermis is complete. Under the thick epidermis of the palms of the hands and the soles of the feet, and under the nails, many of the pustules do not rupture, and must be cut out.

A small-pox convalescent should not be allowed to go out in public until the physician has satisfied himself, by personal observation, that the whole of the skin is free from pustules and from the subsequent desquamation.

The coexistence of small-pox with other acute infectious diseases, each in the acute stage, is very rare indeed. In observations spread over a series of years, including many thousands of cases, I have not seen a single instance of it with the exception of a few cases of small-pox with hooping-cough. Most, if not all, of the recorded cases of coexistence of small-pox with scarlet fever and with measles are instances of scarlatiniform and morbilliform initial rashes. Of course one or other of the acute infectious diseases may occur in small-pox patients during the stage of decrustation and during convalescence.

Erysipelas occurs in the incrustation and convalescent stages of small-pox, but I have not seen it in the acute stage.

Diagnosis.—Difficulties occur, first, in the initial stage; second, in the eruptive stage; and it is not possible, until the initial symptoms have been followed by the characteristic eruption, to make a positive diagnosis of small-pox. Nevertheless, even in the initial stage, if due weight be given to certain symptoms, some approach to a correct diagnosis may be made. Should a person be suddenly seized with headache, severe backache, rigors, epigastric pain, nausea with or without vomiting, and complete anorexia, and should these symptoms be accompanied by high temperature, rapid pulse, and (though not at first) much prostration, one may strongly suspect the onset of small-pox. If, in addition to these symptoms, on the first, second, or third day a petechial erythematous rash appear on the abdomino-crural triangle, with or without its appearance on other flexor surfaces, one may say, almost with certainty, that the disease will prove to be small-pox. A trustworthy history of definite exposure to the infection of small-pox within the usual limits of the incubation period would materially increase the probability of the case being small-pox. But the probability is increased to certainty if on the second or third day of illness there appears an eruption of red macules on the face, extremities, and, to a less extent, on the trunk, which at the time of their appearance, or an hour or two later, are raised, distinctly hard and shotty.

A. *Diagnosis in the Initial Stage.*

In its initial stage small-pox counterfeits certain acute infectious and other diseases, notably scarlet fever, measles, macular syphilides, influenza, typhus, syphilitic roseola, erythemas, rötheln, lumbago, acute nephritis, and menstrual rashes.

Scarlet Fever.—The symptoms common to small-pox and scarlet fever are headache, nausea or vomiting, anorexia, rigors, followed by eruption on first or second day. The pyrexia is of varied degree, the pulse is rapid, respiration is quickened, and in both the skin may be dry.

Symptoms peculiar to Scarlet Fever.—The patient usually complains of sore throat. On examination a bright red ring of faucial injection is seen on the uvula and free edge of the soft palate and pillars of tonsils; and there may or may not be inflammation of the tonsils with dots of exudation on the crypts; perceptible enlargement of the cervical or submaxillary glands is present in the majority of cases; the tongue is coated by a white fur with red, swelled prominent papillæ on a white ground.

Symptoms peculiar to Small-pox.—Severe backache, absence of scarlet injection or inflammation of the fauces such as is usually present in scarlet fever, no enlargement of the cervical or submaxillary glands. The throat may feel dry, but the patient does not complain of it being sore. The tongue may be coated, but its papillæ not enlarged. In ordinary cases of small-pox the temperature is usually higher than in scarlet fever; but in the hæmorrhagic small-pox with scarlatiniform initial rash the temperature is low.

If the initial erythema of small-pox be general, enveloping the skin of the face, neck, trunk and limbs, it resembles the rash of scarlet fever; but on looking closely it will be noticed that the punctate appearance, which is always present on the thighs and arms in the case of bright scarlet rashes, does not appear in the initial erythema of small-pox. In the groins there will most probably be a more marked deepening of the tint of the rash than is to be noticed in scarlet fever. It may, however, be impossible to give a diagnosis from the appearance of the eruption. The fauces should therefore be examined. In a case of scarlet fever with an eruption so extensive and bright there will be marked redness on the soft palate and fauces, and swelling and inflammation of the tonsils. In small-pox these appearances will be absent.

If the erythema be partial, limited to the trunk alone, or to the trunk and flexor surfaces of the limbs, scarlet fever may be excluded by the absence of eruption on the neck and upper part of the chest, by the absence of faucial injection, and of cervical and submaxillary glandular enlargement. The tint of scarlet fever rash is usually brighter than that of the scarlatiniform rash of small-pox; and a large number of cases may be excluded from the difficulty of diagnosis, if the fact be kept in view that these initial scarlatiniform rashes do not occur in children under ten years of age. Partial initial scarlatiniform erythemas present perhaps less difficulty in diagnosis than general scarlatiniform erythemas; but the eruption of scarlet fever occasionally counterfeits the initial petechio-erythematous rash of small-pox so closely that a mistake in diagnosis may readily occur.

Cases of scarlet fever are seen in which, along with typical scarlet inflammation of fauces and enlargement of submaxillary and cervical glands, there is a brilliant scarlet rash, with minute purple petechiæ showing on neck, just above clavicles, and in groins. In such cases it is most necessary that particular care be taken to weigh well the significance of the faucial inflammation and cervical and submaxillary glandular enlargement that are invariably to be noted in these cases; because the minute purple petechiæ in the groins and on the neck are indistinguishable from those that appear in these situations in cases of the hæmorrhagic small-pox with a general bright scarlatiniform initial rash. After examining the throat there should be no difficulty as to diagnosis.

Measles.—Symptoms common to measles and small-pox are—eruption, pyrexia, rapid pulse, anorexia, and in some cases suffusion of conjunctivæ.

Symptoms peculiar to Measles.—Catarrhal symptoms almost invariably the earliest; lachrymation, cough, coryza, for one, two, or three days; minute pink dots on soft palate, fauces, and pharynx, and these may be slightly swollen. The eruption appears on the skin usually on the third or fourth day; it consists at first of minute raised pink dots behind the ears, and on forehead, chin, cheeks, and neck, rapidly showing on the limbs and chest. Measles mostly attacks children under ten. The eruption reaches its height on the second or third day of the rash, that is, on the fifth or sixth day of the disease; it is then composed of large, soft, velvety, raised pink papules, confluent in many parts of the skin. On drawing the fingers across the forehead, the spots, although very distinctly raised and somewhat resistant, are soft, not hard or shotty. The temperature in measles is not high until the rash appears, and it reaches its height with the full development of the eruption.

In small-pox with initial morbilliform eruption catarrhal symptoms are not present, or extremely rarely; and some of the symptoms—such as headache, backache, rigors, epigastric pain, nausea, and vomiting—will be present. This initial eruption appears on the first or second day of illness on the face, trunk, and extremities simultaneously. The spots at first are larger in size than the minute spots of measles, and the eruption has spread over the entire surface of the skin by the time that the eruption of measles is beginning to appear on the face and neck. The eruption is very slightly if at all raised. It disappears in twelve to twenty-four hours after it has reached its height, and does not leave the faintest stain. Before, simultaneously with, or immediately after the disappearance of the rash the papules of small-pox appear and the temperature falls. If the initial morbilliform rash be partial it appears on the groins, sides of trunk, the flexor surfaces, or the extensor surfaces of joints, it is not accompanied by catarrhal symptoms, and having regard to its distribution, should not give any excuse for a diagnosis of measles. In a very small number of cases of measles, on the first or second day of disease, an initial general erythema occurs which is absolutely indistinguishable from the general scarlatiniform erythema of small-pox. It occurs, however, so far as my observation goes, only in children under ten, the age period in which the initial scarlatiniform rash of small-pox does not occur.

Typhus.—Symptoms common to typhus and small-pox are pyrexia, headache, rigors, anorexia, thirst. In typhus there is occasionally an initial erythema on the face and forearms on the third or fourth day, followed by the typhus eruption of red macules on the forearms, chest, abdomen, and limbs on the fourth to the fifth day. Hardly ever does the eruption of typhus appear on the face. The macules are not in the faintest degree hard or raised. In small-pox a shotty, papular eruption as a rule has appeared by the third or fourth day of illness, and with its appearance the high temperature and initial symptoms subside; whereas in typhus the temperature does not fall when the characteristic eruption appears.

Syphilitic Roseola ("Macular Syphilide") appears usually on the trunk and face, soon changing to a raw ham colour; it is not accompanied by initial symptoms of the severity of small-pox, unless it appear just after a debauch, when headache and malaise will doubtless be present. The inguinal, perhaps the cervical lymphatic glands, will be found enlarged.

Influenza.—The points wherein it differs from small-pox are the more sudden seizure and more complete prostration at first; the headache is accompanied by suffusion of the eyes and pain behind them, whilst pain in the limbs is a very prominent symptom. If scarlatiniform or morbilliform rashes accompany influenza, the difficulty of diagnosis is increased. On the third day the course of the disease, and the appearance or non-appearance of a small-pox eruption, will remove any doubt.

In ordinary *Erythemas* neither the initial symptoms nor the initial temperature of small-pox are present. Ptomaine erythemas, due to shell-fish, etc., may present considerable resemblance to small-pox initial rashes, not only in their appearance, but in the rapidity of their development. If there be no headache or backache, and the temperature not much raised, inquiry should be made into the recent diet of the patient. In many instances the cause of the attack may thereby be discovered. In most cases of ptomaine poisoning the onset of the symptoms is more sudden than even in small-pox.

In *Rötheln* the initial temperature and symptoms of small-pox are absent.

Copaiba Rash.—In this there is usually an absence of the initial symptoms and temperature of small-pox.

Lumbago may be mistaken for small-pox, but the absence of fever, the headache, and other symptoms should be sufficient to exclude the diagnosis of small-pox.

Acute Nephritis.—In this disease neither is the temperature raised to such a degree, nor are the headache and backache so pronounced as in small-pox. The scanty secretion of urine containing albumin, the occurrence of œdema, and the absence of small-pox eruption, should remove any doubt as to diagnosis.

Menstrual Rashes.—A general erythema, covering the entire skin of a deep purple colour, and fading on pressure, occurs sometimes in women over thirty at the time of menstruation. The colour is so dark that it has sometimes been mistaken for hæmorrhagic small-pox. Small-pox should without much difficulty be excluded by the fact that the mucous hæmorrhage is exclusively uterine, there being no bleeding from the gums, no epistaxis, hæmoptysis, or hæmatemesis, nor any circular purpuric spots or purple petechiæ on the skin. The eruption is not accompanied by the initial symptoms of small-pox, except perhaps backache, nor by the prostration that invariably attends the hæmorrhagic small-pox.

B. *Diagnosis in the Vesicular Stage.*

Small-pox, when the characteristic eruption is fully out, may be mistaken for diseases that are accompanied by papular, vesicular, or pustular eruptions. These are chiefly measles, chicken-pox, syphilis, eczema, enteric fever, prickly heat, acne, herpes, lichen, glanders, and rheumatic rashes.

Measles.—Confluent small-pox, on the first or second day of the eruption, is frequently diagnosed as measles. The signs that mislead the observer are usually confined to the face and arms, where the skin is often congested, intensely hyperæmic, of a purplish red, studded with large raised papules about the size of the spots of measles. The skin is swollen as in measles, the eyes are most probably suffused, and a careless observer not looking closely may easily be mistaken as to the nature of the disease. In small-pox, however, careful examination will show that the papules are more raised than those of measles, that minute vesicles are forming in the centre of some, if not in many of the papules, and on pressing the fingers of the hand firmly to the forehead and drawing them slowly across, the papules are felt to be resistant, hard, and shotty. In measles there is not a trace of vesiculation, and the eruption, though resistant, is velvety and soft—not in the faintest degree hard or shotty. Further, on examining the mouth and soft palate numerous small, white, vesicular spots are often seen on the mucous membrane in small-pox, but not in measles.

Chicken-pox.—This disease is the one most commonly mistaken for small-pox. Cases of small-pox occurring in unvaccinated children are very frequently mistaken for chicken-pox.

The diagnostic points of chicken-pox are as follows :—

(i.) The initial symptoms. (ii.) The distribution of the eruption. (iii.) The character of the eruption. (iv.) The temperature.

(i.) *Initial Symptoms.*—There is usually complete absence of these in chicken-pox, but occasionally they closely simulate those of small-pox, with this exception, that the temperature is not raised, or but slightly so.

(ii.) *Distribution of Eruption.*—The eruption is most abundant on the trunk and sometimes on the scalp; it is less on face, less still on the arms, thighs, forearms and legs, and least of all on the hands and feet. It is always discrete, and may appear all in one crop, or in successive crops, extending over one, two, three, four, five or more days after the first.

(iii.) *Character of Eruption.*—In all cases of chicken-pox the eruption is at first either macular or papular; but, on account of the absence of symptoms, the eruption in nine cases out of ten is not seen until the vesicular stage. Within a few hours of their appearance the macules have become vesicular. On the abdomen, chest and back many of the vesicles are oval in shape, but in addition there may be a considerable number of circular or irregularly circular vesicles. Those on the face are usually irregularly circular, but on the scalp they are round or oval. On the arms and thighs they are mostly round, with a few oval and elliptical ones here and there. Those on the forearms and legs are almost invariably round, and smaller than those on the trunk; while those on the hands and the feet are even smaller than those on the forearms. The oval vesicles when fully distended by fluid are of an elongated, dome shape, whilst the circular vesicles when full are hemispherical. They are clear, bright, and shiny, and filled with a clear transparent fluid. They are unilocular, and when pricked collapse.

(iv.) Temperature is not at all or only slightly raised before the rash appears, and may or may not rise when the rash comes out; but if it be raised before the appearance of the rash it does not then fall.

In small-pox the initial symptoms are marked, and there is high fever. The eruption is not fully vesicular within six to twelve hours of its appearance; the vesicles when formed are not oval, they are multilocular, and do not collapse on being pricked. The small-pox eruption is most abundant on the face and extremities, and the temperature falls after the appearance of the characteristic eruption.

The diagnosis of chicken-pox must be determined by the distribution of the eruption and the character of the vesicles distributed on the trunk, thighs and arms. In chicken-pox the eruption is most abundant on the trunk, less so on the face, still less so on the forearms and legs, and least of all on hands and feet. This circumstance attracts attention, and, if the eruption be carefully examined, typical unilocular oval vesicles are invariably found on the abdomen, chest, sides of trunk, or back, mixed very often with macules, papules, and small abortive vesicles. All the vesicles in these situations are not by any means characteristic; some are round or irregular in shape. Frequently on the first or second day of eruption some of the vesicles, ruptured by scratching or other means, have partly if not entirely collapsed, and show a small central, amber-coloured scab, which, if the whole of the vesicular fluid have not exuded, rests in the depressed centre of the vesicle, and gives it somewhat the appearance of a depressed small-pox vesicle. In natural small-pox the vesicles do not attain to a hemispherical dome shape on the first or second day of eruption as do the chicken-pox vesicles: this does not take place until they become pustules.

On the extremities the similarity of the vesicles of chicken-pox to those of modified small-pox usually increases in direct ratio to the distance from the trunk. In many cases the vesicles on the forearms, legs, backs of the hands, and back and dorsum of foot, are round and hard, small in size, not unlike the eruption of modified small-pox, and if one regarded only the eruption on the forearms, hands, legs, and feet, it would be impossible in more than half the number of cases to say whether the disease was chicken-pox or small-pox. But all cases of chicken-pox present typical vesicles on either the abdomen, chest, back, thighs or arms.

Cases of small-pox in unvaccinated children have frequently been mistaken for chicken-pox; but if due regard be had to the distribution of the rash, and above all to the fact that in chicken-pox some of the vesicles at least have reached their full development within one day from the appearance of the papule, while in small-pox the vesicles are not fully developed until five days after the appearance of the eruption, no mistake ought to be possible. Mistakes of this nature have again and again been the cause of small-pox outbreaks.

Syphilis.—Usually the scaly papular and pustular eruptions are mistaken for small-pox; in some cases the history of the gradual appearance of copper-coloured scaling papules and the symmetrical distribution will at once suggest syphilis; and further examination of the condition of the lymphatic glands and the history of the case will negative the diagnosis of small-pox. If copper-coloured papules coexist with scaling papules and pustules, a mistake should not be possible, but if there have been high initial fever of a few days' duration, followed by a general papular eruption becoming in part at least vesicular or pustular, the diagnosis may present some difficulty. In most if not in all such cases of syphilitic eruption there are flat, copper-coloured, scaly papules along with vesicles or pustules, and the evolution of the eruption is slower than small-pox. Such a combination never occurs in small-pox, and many mistakes made in the diagnosis of pustular syphilides might be avoided if this fact were carefully noted. If, in addition, the temperature do not fall with the appearance of the eruption there should be no doubt whatever as to the exclusion of small-pox as a possible diagnosis; while the invariable presence of enlarged lymphatic glands, and the history of the case, add to the certainty of its being syphilis, not small-pox; here again an examination of the entire surface of the skin should not be omitted.

Herpes.—A cluster of papules arise on a circumscribed area of inflammation, become vesicular by the end of the first day, are transparent and filled with a clear fluid, and collapse on being pricked. If present on the palate and fauces they look not unlike the vesicles of small-pox, but the distribution of the rash and the absence of the initial symptoms of small-pox ought to remove any difficulty as to the diagnosis of the case.

Eczema.—Here again the initial symptoms of small-pox are absent; the vesicles are small, and arranged on an inflamed base which is larger than the papule of small-pox. The hardness of the inflamed skin is diffuse, not shotty.

Glanders.—If the poison be inhaled, after the usual incubation period has elapsed, there is malaise with pyrexia and pain in the limbs. The eruption is at first composed of red papules; these are indurated and increase rapidly in size till they are about as big as a pea. Pustules form on the top of the papule. There is a fœtid nasal discharge. The initial symptoms and course of the eruption and of the disease are totally unlike the symptoms and course of small-pox; while the severity of the constitutional symptoms is out of all proportion to those that accompany a case of small-pox with a like amount of eruption. Moreover, nasal discharge is almost unknown in small-pox. If inoculated, the local wound, character of the eruption, and the history of the case, suffice to exclude the diagnosis of small-pox.

Pyæmic Skin Eruptions.—Those mistaken for small-pox often occur in cases of ulcerative endocarditis. There is present an eruption of a small number of petechiæ and pustules. The petechiæ vary from the size of a lentil to a split pea, are irregular in outline, of a red tinged with purple colour, and distributed mostly on the extremities; interspersed with these are small pustules. The gradual onset of the symptoms, the date of the appearance of the eruption, its sparseness, the absence of deep violet or purple spots, the continued high temperature, the great prostration and severe constitutional symptoms, negative the diagnosis of small-pox.

Enteric Fever.—If the eruption be present on the trunk, limbs, and perhaps on the face, the rose spots much raised and more or less resistant, or if some of the spots show minute vesiculation, the disease may be mistaken for small-pox. The history, symptoms, and duration of illness, one week at least before the appearance of the rash, should remove any doubt as to the nature of the ailment.

Prickly heat may be excluded by the absence of the initial symptoms and temperature of small-pox.

Iodide Rash.—In this the initial symptoms and fever of small-pox are absent.

Rheumatic Eruptions.—A copious eruption of miliary vesicles occurs in rheumatism and other diseases attended by great sweating. It is most abundant in the trunk. The vesicles may be of the size of a large pin's head, or slightly larger, are closely aggregated, covering the abdomen, chest, and back, and often there is a large number on the extremities. The distribution of the eruption is not that of small-pox: the vesicles are small, hemispherical, filled with a clear or straw-coloured fluid, and collapse on pricking. The history of rheumatism or other disease attended by sweating, the absence of initial symptoms of small-pox before the eruption appeared, its distribution and character, ought to enable one to exclude small-pox.

Acne.—Initial symptoms of small-pox wanting. The eruption is distributed on the face and shoulders. The pustules are acuminated, some of them indurated, and they show a central dot or comedo.

Lichen.—The papules are soft and red, and do not become vesicular; there are no initial symptoms.

Pemphigus.—The initial symptoms of small-pox are wanting; the bullæ are much larger than small-pox vesicles; they are distended by clear, straw-coloured fluid, and collapse on being pricked.

Urticaria papulosa.—The wheals are small, of the size of a split pea, and of a dull white colour; they rise in an hour or two to the full size, either with no redness at the base or that of the usual erythema of urticaria. The vesicle is hard like the small-pox vesicle, but in urticaria it attains the size of a split pea in a few hours; the initial symptoms are not those of small-pox.

Chemical irritants sometimes produce a vesicular eruption indistinguishable from that of small-pox. I have seen a confluent vesicular eruption on the forearms and hands, with a few vesicles on the nape of neck, mistaken for small-pox. The vesicles were of the size of those of natural small-pox at fifth day of eruption. The limitation of a confluent vesicular eruption to the forearms and hands, and complete absence of eruption on trunk and extremities, negatived the diagnosis of small-pox. In addition initial symptoms were absent, and the rash had attained its height within two days from the time that the patient had immersed his arms in a strong solution of washing-soda. The vesicles on the nape of the neck were accounted for by the fact that the patient had scratched the spot with his wet fingers.

To avoid mistakes in the diagnosis of eruptions which counterfeit that of small-pox, be it the natural or modified small-pox, is in all cases perhaps impossible; but a careful examination of the entire surface of the skin, with full inquiry as to the history of the case, will obviate the occurrence of many errors in diagnosis. The great practical importance of the diagnosis, and the anxiety with which doubtful cases are regarded, must be my excuse if I have gone too tediously into this part of the subject.

Prognosis.—A. The general considerations which affect the prognosis of small-pox are age, vaccination, and, in a minor degree, the sex of the patients. The following table shows the fatality of small-pox in unvaccinated and vaccinated patients in the different quinquenniads up to thirty:—

TABLE showing number of Cases, Deaths, and percentage Mortality in different quinquenniads up to Thirty.

	UNVACCINATED.			VACCINATED.		
	Cases.	Deaths.	Mort. p.c.	Cases.	Deaths.	Mort. p.c.
Under 5 years	1131	647	57·2	385	30	7·8
5– 9 ,,	952	385	40·4	1,468	59	4
10–14 ,,	607	155	25·5	3,080	90	2·9
15–19 ,,	385	158	41	4,091	191	4·6
20–24 ,,	276	128	46·3	3,486	321	9·2
25–29 ,,	199	91	45·7	2,079	228	10·9
30 and upwards	390	194	50	3,167	522	16·4
Totals	3940	1758	44·6	17,756	1441	8·1

It will be noted that the age of least fatality in the two classes is 10 to 14. The next most favourable quinquenniads in both are 5 to 9, and 15 to 19. The mortality in unvaccinated cases is between 40 and 50 per cent, and varies from 20 to 30 per cent in quinquenniad 10 to 14, to 50 to 60 per cent under 5, while in the vaccinated at the same periods it is 2·9 per cent and 7·8 per cent respectively.

The character of the vaccination also affects prognosis.

TABLE showing number of Cases, Deaths, and percentage Mortality of Patients with one, two, three, and four or more good and indifferent marks.

No. of Marks.	Character of Marks.	No. of Cases.	Deaths.	Mortality p.c.
One	Good	1,095	70	6·4
	Indifferent	2,044	341	16·7
Two	Good	1,461	54	3·7
	Indifferent	2,476	279	11·2
Three	Good	1,095	41	3·7
	Indifferent	1,778	133	7·4
Four or more	Good	826	23	2·7
	Indifferent	949	46	4·8
	Total	11,724	987	8·1

This table shows that while mortality among cases with one good mark is 6·4 per cent, among those with one indifferent it is 16·7. Among those with two good marks it is 3·7; among those with two indifferent marks it is 11·2. Among those with three good marks it is 3·7 per cent, and in those with three indifferent it is 7·4. Among those with four or more good it is 2·7; among those with four or more indifferent it is 4·8. Good marks are those that show a well-foveated surface, and indifferent are those showing faint foveations or smooth surface.

If efficient vaccination be estimated by superficial area of marks the difference is even more striking. Efficient vaccination is now held to be not less than half a square inch of well-foveated surface, but even with one-third of a square inch of well-foveated surface of 1435 consecutive cases observed by me, only 36 died, giving a mortality of 2·5 per cent; while among 4373 patients with less than one-third of a square inch of well-foveated surface or any extent of non-foveated surface, 378 died, that is, 8·7 per cent. So that the protection against fatal attack is about three or four times greater among patients with efficient than those with non-efficient vaccination.

Should a person who has been successfully revaccinated contract small-pox, the risk of the attack proving fatal is very small indeed, unless small-pox be superadded to some pre-existent serious disease, for example, of kidney, lung, brain, etc. There are, however, some exceptional persons in whom the protection against small-pox afforded by vaccination and revaccination, or previous attack, does not last more than a year or two; and it is impossible in all cases to promise immunity from attack or even from death after vaccination and revaccination. But I have not seen a fatal case of small-pox in any one whose primary vaccination was good (one-third of a square inch), and whose revaccination had been successful.

Sex of Patients.—Small-pox is about 1 per cent more fatal in males than females.

The nature of the prevailing epidemic affects prognosis to some extent; for instance, the epidemic of 1871 was considerably more fatal generally than the outbreaks for some time before or since.

B. Special considerations affecting prognosis.

Serious antecedent or coexistent illness affects the prognosis unfavourably, and small-pox when it attacks tipplers seems often to assume the vesicular or pustular hæmorrhagic form, the prognosis being then most unfavourable.

The duration of the incubation period hardly affords reliable indications as to the severity of the subsequent attack, but some have noted that, in pure hæmorrhagic cases, it is not infrequently shorter than the average.

Considerable assistance in prognosis may be derived, however, from the early symptoms, the appearances presented by initial rashes, the amount of the characteristic eruption, and particularly from the hæmorrhagic symptoms.

Initial Symptoms.—If these be mild the attack will probably not be fatal. But the converse does not hold good, for although in the majority of confluent and in all pure hæmorrhagic cases the initial symptoms are severe, yet severe initial symptoms often usher in a mild attack. If the temperature be not above 100°, and there be dusky or general vivid erythema, the case will probably prove hæmorrhagic and be fatal.

Initial Rashes.—Partial erythemas, unaccompanied by hæmorrhagic signs, indicate every probability of a mild attack. General scarlatiniform and morbilliform erythemas are usually followed by mild attacks, especially in vaccinated subjects. On the other hand, a vivid red general erythema is often met with in patients whose attacks prove to be of the hæmorrhagic type. If a general erythema be accompanied by an abundant crop of purple petechiæ in the groins or elsewhere, the case will probably prove fatal; and if accompanied by isolated ink spots it will certainly be fatal. If partial petechio-erythematous rashes show only the bright red petechiæ the case will probably recover. If, on the other hand, there be masses of purple petechiæ in the abdomino-crural triangle or in the lumbar region the case will most likely be fatal. If a petechial rash be composed of bright red and purple petechiæ, the case is likely to be severe; if vaccinated, the case will probably recover; if unvaccinated, it is not unlikely to end in death. Generally speaking, the probability of a severe attack following an initial rash is directly proportioned to the depth of the purple hue or the degree of the duskiness of the rash. Blood in the urine in the initial stage is an unfavourable symptom, as is also hæmorrhage from mucous surfaces and the uterus.

In discrete modified small-pox the prognosis is very good; death rarely occurs. In discrete unmodified small-pox the prognosis is very unfavourable under one year; less so between one and three years of age; after that good. Convulsions and coma in modified or unmodified discrete small-pox are unfavourable, especially so if they supervene from about the sixth to the ninth day of disease.

Confluent Modified Small-pox.—In vaccinated adults there is not infrequently a copious, almost confluent eruption, and during the first few days it is impossible to say whether or not the case will be modified. On the third day of the eruption, sometimes on the fourth, the vesicles on the face, which is usually at that date in these cases markedly œdematous, show a central opacity or get uniformly cloudy. It may then be safely affirmed that the attack will be modified, and that the patient will, in all probability, recover.

Confluent Unmodified Small-pox.—Gravity of prognosis bears a direct ratio to the degree of confluence of eruption. If quite confluent on the face, head, arms and back, the patient rarely recovers; but if the eruption be not confluent on the back the chance of recovery is much greater. The eruption on the abdomen is usually discrete in confluent cases. Under two years of age confluent natural small-pox is almost invariably fatal; from two to five years about one-fourth of the cases recover; the prognosis thereafter is more favourable, and from ten to fourteen the patient is more likely to recover than at any other age. After fifteen years of age the percentage of deaths to recovery increases steadily with advancing years.

In all cases, abundant eruption on the mouth, fauces, and pharynx is an unfavourable symptom; and if symptoms of laryngeal obstruction supervene, the gravity of the prognosis is increased. Subcutaneous œdema is not in itself unfavourable; on the contrary, if the vesicles fill with lymph very slowly, and the skin at the fifth or sixth day of eruption presents a flat, pasty white, or rough parchment appearance, accompanied by very little swelling (other than that caused by the raised epidermis), the prognosis is most unfavourable, recovery rarely taking place, and, as a rule, only in patients between ten and twenty years of age.

Delirium in the vesicular stage, and, in children, grinding of the teeth, are unfavourable. If the temperature in the vesicular stage do not fall under 100° the prognosis is less favourable than if it fall to normal. A temperature over 104° in the pustular stage, attended by restlessness and delirium, is unfavourable; and if much dermatitis, deep cellulitis, laryngeal or pulmonary complications, or diarrhœa be present, the gravity of the prognosis is heightened.

Hæmorrhagic Small-pox.—True hæmorrhagic small-pox is invariably fatal. Where hæmorrhagic symptoms and the eruption of small-pox co-exist, the prognosis becomes less grave as the purely hæmorrhagic symptoms diminish, and the case more nearly approaches the form in which these are limited to sub- and peri-vesicular hæmorrhages; but in all these cases the prognosis is exceedingly unfavourable, and recovery very rarely takes place.

In sub- and peri-vesicular hæmorrhagic cases, if the eruption be discrete and hæmorrhage appear late and be limited mostly to the lower extremities, recovery is to be hoped for; but if the eruption be abundant, and sub- and peri-vesicular hæmorrhage general, recovery is very doubtful. If the eruption be confluent with general sub- and peri-vesicular hæmorrhage, recovery does not take place; but many confluent cases recover if hæmorrhage be present only in the lower extremities, and to a limited extent on the trunk and arms.

The presence of a claret-coloured areola encircling the majority of the vesicles early in the course of eruption is a most unfavourable sign. It often appears on the second day of eruption, and affords early evidence as to the probable termination of the disease. If it be present on the lower extremities only, it is not in many cases of much significance. In all forms of hæmorrhagic small-pox copious hæmorrhage from the mucous membranes deepens the gravity of the prognosis.

The appearance of serious lung complication during the pustular and incrustation stages is unfavourable, as are also extensive erysipelas of the extremities and deep cellulitis.

The age of the patient and the character of the vaccination must in all cases be regarded when forming a prognosis.

Morbid Anatomy.—*Skin.*—In the earliest stage of the eruption the first change is a circumscribed hyperæmia of the papillæ of the cutis. The cells of the rete Malpighii very soon begin to swell, the upper layer of the epidermis is raised, and the papule is formed. Serum exudes from the papillary layer, and by its pressure on the swollen cells these become elongated, and to some extent separated, but they still cohere by parts of their surfaces. In this way is formed a sort of filamentous network connecting the raised portion of the epidermis with the papillary layer underneath; into the vacuoles or loculi of this network the serum exudes, and at first into the central portion of the papule. Slowly, day by day, the vesicle enlarges at its periphery, where the serum is exuded in larger quantity than at the centre of the vesicle. Hence the walls of the vesicle at its periphery are raised above the level of the central portion, and the central depression or umbilicus is formed. This is the characteristic mode of growth of a vesicle, but a central depression is not present in every instance.

Rindfleisch and others believed that a hair follicle or sweat gland was the cause of the central depression; that these have only an accidental relation to the depression is shown by the fact that the vesicles on the glans penis, where there are no hair follicles, show a central depression; and many vesicles, in the periphery of which a sweat gland or hair follicle is situated, are as regular in outline and show as typical a central depression as those in which one or other of these is situated in the centre. When the vesicle has attained the limit of its growth (five days), leucocytes, which are present in small numbers from the first, increase in number in the centre of the vesicle, which on the fifth to sixth day shows a central opaque dot. They gradually invade the whole of the vesicle, the serum becomes turbid, and in three days the vesicle is filled with pus. In many confluent cases pus cells infiltrate the deeper layers of the rete Malpighii and upper layer of the cutis, dermatitis ensues, the blood-vessels of the cutis are compressed, and limited areas become necrosed. The crusts and necrosed portions separate after a time, the ulceration of the cutis heals slowly, and the resulting cicatrices bear a direct ratio to the depth and extent of ulceration. In many cases pus is limited to the pustule and the middle layer of the rete Malpighii. The pustule ruptures and discharges its contents, or it dries unruptured. New epidermis forms underneath, and the crust falls off, exposing a red, healed epidermal surface, which is raised, flat, or slightly depressed.

If there be no ulceration of the cutis there is no pitting; though there may be a temporary depression due to the flattening of the papillæ. In a considerable number of cases of natural small-pox, owing to hypertrophy of the papillæ at the site of the pustule, an elevation of skin results as soon as the crust has fallen off; the new discoloured epidermis, being well raised above the level of the unaffected skin, imparts to it a nodulated, in many cases a tubercular appearance, usually most marked on the face. After a time the hyperæmia subsides, the nodules shrink, and the skin in many cases regains its natural colour and smoothness.

Mucous Membranes.—Vesicles are formed by infiltration of serum in the middle epithelial layer with subsequent purulent infiltration of the vesicle and of the lower layers, and sometimes of the submucous tissue. The amount and depth of ulceration of the pustules on the mucous membranes are often in direct proportion to the ulceration and purulent infiltration of the cutis. The mucous membrane of the larynx, if eruption be present, is injected and swollen, and shows minute ecchymoses, accompanied by free muco-purulent secretion.

Some authorities state that a diphtheritic condition of the fauces and pharynx occurs not infrequently. This appears to me to be a mistake.

In cases with a large amount of eruption on the fauces, pharynx, and palate, the swollen tissues, with ragged shreds of mucous membrane and epithelial débris, often present an appearance not unlike the dirty disintegrating membrane seen in diphtheria. I have not seen faucial diphtheria complicate small-pox, nor have I seen a case of small-pox followed by the paralytic sequels of diphtheria. I have noted membrane in the larynx in one or two cases, and once in the trachea.

Vesicles are found on the lips, tongue, buccal mucous membrane, gums, hard and soft palate, tonsils, posterior nares, pharynx, epiglottis, larynx, and trachea, as far as the bifurcation and occasionally beyond; also on the lower part of the rectum, the anus, the vulva, the lower portion of the vagina, the scrotum, the penis, and also on the conjunctiva; but never on the cornea.

Lungs and Pleuræ.—Bronchitis, with copious mucous or muco-purulent secretion, occurs in the majority of severe cases. The lungs are frequently congested, sometimes uniformly so, but perhaps in most cases the congestion is hypostatic. Pneumonia is usually lobular, not infrequently lobar. Lobular pneumonia is of very frequent occurrence in unvaccinated children during the stages of pustulation and incrustation. Pleurisy and empyema generally occur during the stages of incrustation.

The *heart* is flabby and pale, and presents the ordinary signs of degeneration.

Abdominal Organs.—The liver may be, but usually is not congested. It is pale, soft, and shows considerable amount of fatty degeneration, with infiltration of leucocytes between cells of lobules and into interlobular spaces. Occasionally there is thrombosis of minute vessels. The spleen is swollen, the Malpighian bodies enlarged, the pulp soft and infiltrated with leucocytes. In rare cases there are emboli. The kidneys often show swelling of the cortex accompanied by fatty change. The intestinal mucous membrane, especially that of the small intestine, is congested; and there may be congestion and swelling of Peyer's patches. Sometimes ulceration of the intestine occurs, probably due to minute emboli. The testicles in some cases show parenchymatous inflammation without effusion into the tunica vaginalis; in other cases there is inflammation of the tunica vaginalis with fibrinous effusion.

The *muscles* show granular and fatty degeneration.

The changes in the heart, liver, spleen, kidneys, testicles, and muscles take place during the pustular and incrustation stages. The blood is dark in colour, and coagulates slowly and imperfectly. There is some degree of leucocytosis in the pustular and incrustation stages, but not more than in some of the other acute infectious diseases.

Brain.—Occasionally cerebral apoplexy occurs by rupture of a vessel, and a large quantity of blood is extravasated.

In fatal cases of coma nothing is noted except congestion of the meninges, and in some cases hæmorrhage under the pia mater. Zuelzer has observed hæmorrhages into nerve-sheaths, and it is not improbable that some of the nervous sequels may be due to minute hæmorrhages in the cerebrum and spinal cord. In some cases of paraplegia small focuses of softening have been found in the gray and white substance of the cord.

Morbid Anatomy of Hæmorrhagic Cases.—Where sub- and perivesicular hæmorrhage takes place, it is into the whole thickness of the cutis; but the serum exuded from the hæmorrhagic surface is nearly always free from hæmoglobin or blood corpuscles.

The purple petechiæ, and the inky or deep violet coloured circular spots, are caused by hæmorrhage into the whole thickness of the cutis; sometimes the hæmorrhage extends to the subcuticular tissue. It is probable that these skin hæmorrhages are due to transudation of the red corpuscles through the walls of the capillaries. The bruise-like swellings are caused by hæmorrhage into subcutaneous and intermuscular connective tissues.

Subconjunctival and retinal hæmorrhages occur. Deep-seated hæmorrhages take place into the muscles, connective tissue, and mediastinum. Subpleural hæmorrhages—visceral, parietal and diaphragmatic—and hæmorrhages into the lung substance, are common. Subperitoneal hæmorrhages occur on the surface of the liver, spleen, pancreas, mesentery, and large and small intestine. Extensive extravasations of blood take place into the loose tissue and fat round the kidneys, and extend along the course of the psoas muscle into the pelvis. Hæmorrhages into the liver and spleen are very rare.

Kidneys.—Subcapsular hæmorrhages are of frequent occurrence, but hæmorrhage into the cortex and pyramids is very rare. There is often a copious extravasation of blood into the tissues between the calices and the substance of the kidney, whereby the calices are compressed, and some of them detached from the papillæ, the space being filled with blood. On making a longitudinal section of the kidney the blood-clot appears to fill the calyx and pelvis. On closer examination, however, it is seen that it lies not in the calices and pelvis, but between these and the kidney substance.

Hæmorrhages occur into the mucous coat of the bladder, uterus, vagina, Fallopian tubes, ovaries, testicles, and bone marrow.

Digestive System.—Hæmorrhage occurs into the mucous membrane of mouth, pharynx and nose. In the stomach there are often masses of small red and purple hæmorrhages in the mucous and subcutaneous coats, being especially abundant along the small curvature. They occur in the large and small intestine, and also on the rectum.

Heart and Blood-vessels.—In pure hæmorrhagic cases the heart is contracted, firm, and dark brown in colour. The cavities contain little if any blood or clot, and the arterial trunks are usually almost empty. Hæmorrhages occur under the pericardium and endocardium, but not, so far as I have seen, in the valves or blood-vessels. The spleen is small, firm and dark. The liver is also dark and not enlarged.

Treatment.—The majority of cases of discrete modified small-pox require little beyond rest in bed for a short time, with such food and nourishment as the patient wishes; but cases of severe small-pox require most careful nursing and unremitting attention. There should be an ample supply of fresh, cool air. The temperature of the room should not be under 55° F., nor much above 60° F. The patient ought not to be exposed to draughts. The air in the room should be changed at least four times every hour, and there should be no curtains or hangings to impede its free circulation. The bed and body linen should be of fine soft material, and the coverings light. A hair mattress on wire makes the most comfortable bed. No matter how fine the linen, the pressure of the bed-clothes and the mattress make the patient feel as if he were sleeping on thorns. Some relief may be afforded by a water-bed, but air and water cushions are useless.

Nourishment, Diet, and Stimulants.—The nourishment should be light and suitable. In the initial stage many patients take little nourishment, nor is it necessary that they should take much more than milk and water, with tea, coffee or aerated waters. During the vesicular and pustular stages beef tea, light broths of veal, chicken, or mutton, arrowroot, eggs, jellies, boiled custards, should be added. Ice is very agreeable to most patients, and water should be given freely. In many cases, especially in children, peptonised milk is most useful.

In all cases nourishment should be given frequently, and if possible not in too large quantities at a time; but thirst is often excessive and unquenchable, and enormous quantities of fluid are drunk.

During the initial and vesicular stages alcoholic stimulants are not required, unless it be in exceptional cases attended by much cardiac weakness and prostration. During the pustular stage and period of scabbing alcohol is often of decided benefit. The indications for its use are prostration and weak, rapid, compressible, or intermittent pulse.

Vesicular and pustular hæmorrhagic cases, as well as some confluent cases, require alcoholic stimulants in the vesicular stage; the chief indications are those just mentioned. Alcohol may be given to all pure hæmorrhagic cases from the commencement of the disease, but it is well to bear in mind that, as recovery from that form of small-pox is unknown, the stimulant is given only to prolong life, not to save it.

The best alcoholic stimulants for the acute stage are good grape brandy, whisky, or champagne. It is useful to vary the kind of stimulant after a time, and to direct that the quality be thoroughly good. In convalescence wine is very beneficial, and port is perhaps the best. To those in the habit of drinking malt liquors, stout and bitter ale may be given with advantage. Iron, quinine, and cod liver oil are useful in convalescence from severe attacks.

The patient may be allowed light food—fish, chicken, boiled mutton, and so on—as soon as the appetite returns; and a few days later the ordinary diet of health may be resumed. In severe cases the appetite may have to be tempted at first by oysters, light puddings, poached eggs, omelettes, spring chicken, or any dainty dish that is likely to be agreeable; as it improves, the ordinary diet of health can be taken.

Nursing.—Careful and judicious nursing, with the most scrupulous attention to the cleanliness of the bed-linen, are all-important. The pus oozing from the pustules very quickly soils the personal and bed linen, which should therefore be changed very frequently. The mouth and nose should be frequently cleansed, and above all the eyes should be watched constantly, and be bathed and cleansed systematically and thoroughly. It is impossible to overrate the importance of this attention.

The handling of the patients must be most gentle, and in raising the head or shoulders the nurse's arm should always be placed under the pillow. Infants, when being nursed in the arms, should rest on a pillow on the nurse's arm. Attention to small details of this kind add much to the patient's comfort.

In the acute stage it is not practicable to wash patients suffering from severe or even moderately severe small-pox; but the skin should be cleansed as much as possible by sponging, and such ablutions as will readily suggest themselves to an intelligent nurse; baths should be given as soon as the patient can bear them.

It is perhaps in the management of delirious patients that the most trying part of small-pox nursing arises. Such patients require most careful and constant watching. Very often they seize the occasion of the nurse's temporary absence and make their escape through door or window. For this reason they should not be left unattended for an instant. In the most common form of delirium the patient has the strongest objection to being considered ill, and insists upon having his clothes given him. A judicious nurse will endeavour to distract his attention, talk to him, humour him as much as possible, tell stories, prevaricate, do anything but argue with or contradict him; and must never, except in some extremity, use mechanical restraint. A delirious small-pox patient, when thoroughly roused and angry, will not hesitate to knock the nurse down and make his escape. In the case of patients whose delirium cannot be controlled by drugs, a useful device is to dress the patient in a dressing-gown, stockings, and slippers, and allow him to walk up and down the ward or round the room, the nurse holding the patient's arm, at the same time keeping her eye on the door and window. Very often the patient after a few turns, finding that he is unable to continue the exercise, is glad to get back to bed. But in many cases it is necessary to have the assistance of an additional nurse or male attendant. If the bedroom be on the first floor or above, stops should be fixed in the sash grooves, so that neither sash can be opened wider than six inches.

Drugs.—In the routine treatment of small-pox opium is invaluable. Not only are rest and sleep induced by it, but a moderate degree of comfort is obtained for the patient during the painful stages of vesiculation and pustulation. In cases where opium may be contra-indicated sulphonal or paraldehyde should be given. The vomiting of the initial stage is often persistent, but morphia will probably relieve, if it do not entirely check it.

To quiet the patient and reduce the delirium it is often, if not invariably, necessary to have recourse to hypnotics, and the best is opium or morphia. If the patient will swallow it, opium may be given by the mouth; but it is preferable, I think, to give hypodermic injections of morphia. Large doses have usually to be given—half a grain of morphia repeated in an hour or two if delirium continue, and again if necessary. In many cases it acts like a charm, and the patient becomes quiet and sleeps for a few hours. But in very severe cases, especially in the mixed hæmorrhagic and pustular, it is often impossible to control the delirium completely by the administration of drugs.

In "black" cases hazeline and ergot may be given with the view of checking hæmorrhage; little or no benefit, however, is likely to result.

Various agents, such as thymol, eucalyptus, or xylol, have been given in the hope of checking the pustulation of the vesicles, but, so far as my experience goes, without effecting the purpose. Not only did these drugs appear to me to be useless, but they had the added disadvantage, in many cases, of making the patient sick.

For bronchitis expectorants sometimes appear to be useful.

Cold baths may be administered during the stage of pustulation with the view of reducing temperature and lessening dermatitis. As in enteric fever, the duration of the bath should be ten to twenty minutes, and the temperature for adults 80° F., reduced to 75° or 70° F.; for children 85° F. reduced to 75° F. The baths must be given with the greatest care, and only in severe cases. Cold baths for the pyrexia of the initial stage are unnecessary.

Constipation should be relieved by agreeable but effective laxatives, aided if necessary by suitable enemas. Diarrhœa, which usually occurs only in severe cases, may often be checked by opium, and with it may be combined such astringents as chalk and catechu.

Local applications are of the utmost importance to allay the excessive irritation of the skin, to lessen the subcutaneous œdema, to favour the separation of the scabs, to clear away the pus as it oozes from the pustules, and to diminish the ulceration and subsequent pitting of the skin. The application of cold compresses, changed every ten or fifteen minutes, sometimes alleviates the discomfort and irritation due to a confluent eruption; but in confluent cases the irritation is often irremediable. Oils and other preparations often add to the patient's discomfort. Astringent applications, such as solution of nitrate of silver, have been used, but I have not been able to satisfy myself that they are of the slightest value. Astringent dusting powder is agreeable to some patients, but many prefer to have no applications whatever on the skin.

Where the eruption is quite confluent, and the patient tears the epidermis off extensive surfaces, it is necessary to muffle the hands, and the oozing cutis should be covered by some suitable cold moist dressing. In all cases where the eruption is copious on the scalp the hair should be cropped short early in the disease.

The early separation of the crusts, whether on the face, scalp, or elsewhere, is most desirable, and can be best accomplished by the application of linseed meal poultices. On the scalp a thick poultice, with iodoform on its surface, may be applied in the ordinary manner; but on the face the method most agreeable to the patient is as follows: Cut a mask of a single thickness of lint, with apertures for the eyes, nose, and mouth; smear a thin layer of linseed poultice on this, taking care to put on the surface a little vaseline in which iodoform has been mixed (greasy applications do not at this stage irritate the patient), and apply it to the face, changing it at least every two hours. By this means the crusts may be separated more rapidly than by any other. It is important that the crusts should be separated from the face as soon as possible, in order that suitable antiseptic dressings may be applied to the ulcerating surfaces. On the arms, legs, and elsewhere, boracic or other moist antiseptic dressing will probably be sufficient. The importance of these moist applications in the incrustation and decrustation stages cannot be overestimated; in this stage on no account should powder be applied to the skin, as it does but aggravate a condition that it is most desirable to subdue.

During the stages of incrustation and decrustation tepid baths one-half to one hour in duration may be given daily, with the view of facilitating the separation of the crusts and cleansing the skin of the trunk and limbs.

The verrucose condition of the skin on the face which occurs in some cases may be lessened by paring off the ragged warty excrescences.

The nose and mouth must be kept clean by spraying, syringing, or swabbing with such lotions as, ℞ Acid. boracic; Liquor sodæ chlor.; Creolin (1 part in 80 of water, and for children rather weaker): or ℞ Liq. hydrarg. perchlor. (1 in 1000): a good mouth wash is one composed of Liq. potassæ and Acid carbol. pur., 1 part of each to 80 of water, diluted if necessary.

Multiple superficial abscesses should be opened as soon as they arise; those on the scalp by crucial incisions: iodoform poultices or warm antiseptic dressings are then to be applied. Deep-seated abscesses should be opened as soon as the presence of pus is detected.

Cellulitis, if extensive, must be incised freely, deeply, and early, and antiseptic fomentations applied.

For laryngitis a steam tent with warm inhalations should be used. If dyspnœa be great, or œdema of glottis occur, tracheotomy should be performed. Owing to the great swelling of the neck in small-pox the performance of tracheotomy is rendered somewhat difficult, and much hæmorrhage may take place.

Glossitis, if slight, subsides without interference. In any case the application of ice is grateful; but if the swelling be very great, it is necessary to make a free incision about half an inch deep and about two-thirds of an inch externally to the raphe.

If erysipelas occur, the affected part should be enveloped in cotton wool, or painted with a paste made of milk and a little liq. plumb. subacetatis: opium must be given to induce sleep.

Cauterisation of the vesicles has been resorted to for the purpose of preventing pitting, but it is a useless and barbarous proceeding.

With the view of arresting the progress of vesicular growth and pustulation, vaccination has been recommended after the appearance of the characteristic eruption. It does not affect the progress of the eruption in the slightest degree.

Eyes.—It is most important that the eyes be kept free from discharge. Chemosis of the lids, often excessive, renders this exceedingly difficult, especially in young children; but much may be done to alleviate if not to prevent some of the complications that are dangerous to the eyesight. Conjunctivitis and ophthalmia usually yield to the applications used for these affections. Particular care should be taken that oil or vaseline be frequently applied to the edges of the lids. For simple corneal ulcer an ointment composed of Hyd. ox. flav. 2 grs., Atropine 4 grs., Petrolatum 2 drms., should be applied to the eye twice a day.

Inflammatory keratitis is usually accompanied by considerable increase of intra-ocular tension and contraction of the pupil, and sometimes by hypopyon. If paracentesis be performed, it may be necessary to repeat it several times. Should a portion of the cornea slough, and perforation result, in favourable cases a small piece of iris may block the opening, but in others a large anterior staphyloma may result.

For non inflammatory keratitis warm (90° to 104° F.) poppy fomentations should be applied every five minutes, and intermitted for one quarter in every hour, until moderate inflammation of the conjunctiva and inflammatory reaction of cornea is set up. Atropine should be dropped into the eye twice a day. As a rule, in this form of keratitis there is no increase of tension; but if there be, a paracentesis or iridectomy should be performed. The application of pressure bandages is very useful. If the eye become completely disorganised excision of the eyeball may be necessary.

The prevention of small-pox is most efficiently ensured by vaccination and revaccination, and the prompt isolation of the sick. Should small-pox break out in a family all those not affected should be revaccinated at once. If revaccination be performed within three days of reception of infection, and if it be successful, none of those exposed to infection will develop small-pox; if done later it may or may not modify the attack.

JOHN MACCOMBIE.

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J. MacC.

MUMPS

Synonyms.—Lat. *Cynanche parotidœa*, *Parotitis epidemica*;
Fr. *Les oreillons*; Germ. *Ziegenpeter*.

Mumps, or contagious parotitis, is one of the milder specific fevers, and occurs for the most part in epidemics. It is most common in children between the ages of four and fourteen, but is seen, although less often, in older persons. The disorder is a highly contagious one; but although a cause of considerable temporary discomfort, is rarely dangerous to life. Still, as consequences of a more or less serious nature may arise from it, it is unwise to treat even slight cases with indifference.

The incubation period, according to the report of the Clinical Society (11), may vary from fourteen days to twenty-five. When the complaint begins it is infectious from the very first, and can be communicated while the patient is merely ailing and before any signs of glandular swelling are to be detected. Its duration is ten days to a fortnight, but the patient must be considered unsafe to others for at least a week longer.

Morbid Anatomy and Pathology.—The inflammation attacks the salivary glands, and is believed to spread from the duct to the substance of the gland. It causes infiltration into the cellular tissue around, but rarely ends in suppuration: when the complaint is at an end the gland is left uninjured. In the orchitis, however, which is apt to occur in mumps, the testicle may afterwards atrophy. In these cases the intercanalicular tissue is little altered, but there is a parenchymatous as opposed to an interstitial sclerosis. The tubules are alone affected, and show marked hypertrophy of their basement membrane, with atrophy of their epithelial lining and disappearance of their lumen.

Mumps is probably due to a microbe. Pasteur found in the blood rod-shaped bacteria, but failed to reproduce the disease with them; and Bordas describes a micro-organism which, he states, is developed in large numbers in the blood as early as eight hours after the beginning of the illness.

Symptoms.—The local affection may be the earliest sign of ill-health, but this is uncommon. As a rule there are premonitory symptoms, and the complaint begins with fever, often accompanied in the child with headache and vomiting. The patient looks and feels ill, and the temperature rises to 102° or 103° F. In a few hours stiffness is complained of in the jaw, and there is aching and tenderness on one side in the hollow beneath the ear. This part is soon noticed to be full, so that the depression disappears; and as the swelling spreads forwards and backwards from this point it comes to involve the greater part of the side of the face and neck. The skin over it may be pale or have a pinkish tint, and the part is tense, elastic, and very tender. The inflammation may remain limited to the parotid first attacked; but usually it spreads to the other side of the face, to the salivary glands beneath the jaw, and sometimes to the fauces and tonsils. The face is then curiously widened, and the prominence of the chin is lost in the swelling of the neck. The disease takes three or four days to reach its height, for, as a rule, the glands are involved one after another. When fully developed there is no change for a day or two; then the swelling begins to subside, and by the tenth or twelfth day all fulness has disappeared. The length of the attack depends upon the quickness with which the glands successively take on the morbid action. It is rare to find the inflammation at its height at the same time on both sides of the face. Often after the subsidence of the swelling on the one side a distinct pause occurs before the other side begins to suffer; and it may happen that the latter becomes affected only after an interval of weeks, as if from a veritable relapse.

All through the earlier period of the illness, and until the swelling begins to decline, the aching of the jaw continues and is increased by movement; so that mastication is painful, and even the acts of speaking and swallowing add to the patient's discomfort. On this account saliva tends to collect in the mouth, but there is no increase in the salivary flow; indeed, as the swelling subsides, secretion for the time may be suppressed (2), leaving a troublesome dryness of the mucous membrane. Sometimes the temperature declines on the second or third day, but it generally remains high until the complaint is fully developed, and then falls more or less abruptly to the normal level.

The above is the ordinary course of an attack of mumps; but the symptoms may be much less striking. Often, especially in sporadic cases, the swelling is insignificant, with little feeling of illness; or, with much swelling and local discomfort, the temperature is normal, and the general health hardly disturbed; or, again, the constitutional symptoms are severe, with little swelling or pain in movement.

Complications.—A remarkable feature of the complaint consists in the so-called metastases which sometimes occur, chiefly in adult patients. These secondary lesions are inflammatory in their nature, and should be regarded rather as further manifestations of the virus than as true metastases. The most common of these complications, in the male subject, is orchitis; in the female the breasts inflame, or there is œdema of the external genitals, or perhaps swelling and tenderness of the ovaries and enlargement of inguinal glands. In exceptional cases orchitis may occur as an early symptom before any swelling is noticed in the parotid gland; but usually it comes on towards the end of the attack; or even after all signs of swelling have disappeared from the face. With the pain of the inflamed organ there is usually a rise of temperature and a return of the feeling of illness, but sometimes the only complaint is of local discomfort. If an interval of apparent health have followed the subsidence of the parotid swelling, the appearance of the complication may be preceded or accompanied by more serious signs of general disturbance. There may be high fever and delirium, or obstinate vomiting and purging, or alarming symptoms of prostration.

The orchitis lasts from three to five days, and is sometimes followed by very rapid atrophy of the testicle. Many instances of this untoward sequel to the inflammation are recorded by French writers. Thus, Lereboullet refers to the case of a young soldier of twenty-two in whom orchitis began on the fifth day of the mumps. The inflammation soon subsided, but was followed by such rapid wasting that in three weeks the affected gland was reduced to the size of a haricot bean.

The above is not the only form of metastasis met with. Sometimes the orchitis is followed quickly by signs of inflammation of the membranes of the brain. This complication is a rare one, but many cases are on record. Although serious enough in appearance, it can be treated with considerable hopes of success. Thus, Dr. G. H. Dowdney has recorded the case of a man aged thirty-five who, during an attack of mumps, exposed himself to chill by driving ten miles in an open trap. This took place on the fourth or fifth day of his illness. On the next day (the fifth or sixth) orchitis began; and the first signs of meningitis were noted on the day following. The man was seriously ill for some weeks, but eventually recovered. A very similar case in a boy of fifteen is narrated by Dr. Monro. Here also the meningitis was preceded by orchitis, and although in the end recovery was complete, the boy was left for a time with unsteady gait, difficult articulation, and marked agraphia. From these latter symptoms it would seem that the inflammation is not always limited to the cerebral coverings. Drs. Lannois and Lemoine have described a case in which aphasia and localised paralysis of one arm followed such an attack and lasted five days. In another case aphasia combined with right hemiplegia persisted for several months. They suggest that to produce such consequences the attack must have consisted really of a meningo-encephalitis, the inflammation having spread from the membranes to the substance of the brain.

The nervous sequels in mumps are not confined to cases which begin with such violent symptoms. As in other forms of acute specific disease, nervous derangements of more obscure mechanism may be met with. Thus, Joffroy has reported a case of generalised paralysis with loss of deep reflexes, but without cerebral symptoms, which he attributed to peripheral neuritis; and Jalon one of optic neuritis with subsequent atrophy of the optic nerve. Dr. R. Percy Smith, too, has known acute mania to follow an attack of mumps.

A temporary facial paralysis is sometimes met with: this seems to be due to direct extension of the inflammation to the sheath of the facial nerve, although it may happen in cases where there has been little parotid swelling and but slight local discomfort. In a case kindly communicated to me by Dr. A. Maude, the local symptoms of mumps were mild, but the general symptoms were of exceptional severity. The facial paralysis was first noticed in the third week, and lasted nearly a month; there was no deafness or otorrhœa.

Other complications are sometimes met with which may vary according to the prevailing type of the disorder. Thus, in one epidemic cases of gastro-intestinal derangement are noticed with abdominal pains; in another epistaxis is common; in a third there are occasional cases of endocarditis (4). Albuminuria, with or without bloody urine, has also been noted. Still, with regard to this matter of complications, it may be repeated that as a rule the course of the complaint is simple and mild, and that secondary disorders are rare if common prudence be exercised in the management of the case.

Perhaps one of the least unfamiliar consequences of mumps is deafness of one ear. This infirmity may come on in the course of the complaint or later. It occurs in two forms. In the first the inflammation spreads through the Eustachian tube to the middle ear. In this case the hearing is usually restored by treatment. In the second, the deafness begins suddenly at an early period of the illness owing, it is thought, to an inflammatory process set up in the labyrinth or cochlea, or both. The middle ear is unaffected. The attack of deafness may be accompanied by noises in the head and sometimes by pain. If the labyrinth be the seat of the lesion there is also vertigo with nausea and vomiting. In this form treatment can do little, and the deafness is generally permanent. As it is usually confined to one side, and may give rise to no pain, the damage to the organ is often discovered only by accident.

Diagnosis.—Mumps is a primary complaint, and is therefore easily distinguished from the non-specific parotitis (parotid bubo), which is always a secondary disease, and occurs as a complication of many forms of acute illness. Symptomatic parotitis (as it is called) may attack both sides of the face, but, unlike mumps, it always ends in suppuration.

In a very mild attack of mumps, if orchitis occur, there is danger of the primary disorder being overlooked through the prominence assumed by the complication. Therefore, in an epidemic of mumps a case of orchitis should always suggest a careful inquiry and examination of the face.

Treatment.—However mild the attack may be, quiet and rest should be strictly enjoined, as the complications and unpleasant consequences of the disorder are due mainly to imprudences committed during its course. On this account they mostly occur in the milder cases, where the general symptoms are trifling with little local discomfort.

The patient should be confined to his bed while the fever lasts, and when the temperature falls should still keep the house until all local symptoms have subsided. The food should consist of strong soups, meat jellies, pounded meats, milk, eggs beaten up, and the like—such things as need no mastication. If necessary the liver must be relieved by a mercurial purge; or, if there be a foul tongue and much gastric derangement, an aperient draught of rhubarb and heavy carbonate of magnesia may be given, flavoured with cardamoms, chloric ether and peppermint water. For local treatment hot bread poultices should be applied, and frequently renewed; or the part may be anointed with a salve composed of extract of belladonna and glycerine in equal proportions and covered with a layer of cotton wool. It is well to cleanse the mouth and throat with an antiseptic gargle several times in the day. A very grateful application for this purpose is made by dissolving salol to saturation in an ounce of rectified spirit with forty drops of chloroform. Thirty to forty drops of this solution added to a tumbler of warm water make a wash pleasant to use and strongly antiseptic.

Of the complications—orchitis is to be treated by warmth and support. If meningitis occur, leeches to the temples followed by ice to the head and aperients must be resorted to. The alarming constitutional symptoms sometimes noticed before the onset of the complication generally cease when the latter shows itself. If there be great prostration, stimulants must be used and warmth applied to the extremities.

EUSTACE SMITH.

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E. S.

WHOOPING-COUGH

SYNONYMS.—Lat. *Pertussis infantum*; Fr. *Coqueluche*; Germ. *Keuchhusten*.

WHOOPING-COUGH, an acute and highly infectious complaint, occurs, like other zymotic diseases, in epidemics, and runs a definite course. Its special characters are severe general catarrh of the air-passages combined with laryngeal spasm and other signs of nervous disturbance. The complaint usually attacks children, and is rarely seen twice in the same individual. It is therefore uncommon to find a grown-up person suffering from it; but young and middle-aged adults, and even quite old people, may sometimes be affected. In them the symptoms are much the same as those noticed in the child, but there is a less tendency to dangerous complications.

Etiology.—Whooping-cough is undoubtedly the result of a specific virus, and many attempts have been made to determine the nature of the infecting agent. Examination of the sputum during the convulsive stage has proved the existence of various kinds of micro-organisms. Carl Burger, of Bonn, found an elongated bacillus, isolated or in chains; and Afanassieff made cultures of a similar microbe, and injecting this into the windpipe of dogs and rabbits, succeeded in producing symptoms exactly resembling those of pertussis. Ritter examined the sputum from the bronchi and lower third of the trachea, and discovered very small diplococci, which were often arranged in straight or clustered chains. He, too, succeeded in cultivating the microbe, and could reproduce the disease with it in dogs. Unfortunately this result is not conclusive as to the real nature of the organism, for in the dog it is said that various agents will set up an apparently typical whooping-cough. A streptococcus which forms both long and short chains has been discovered by Cohn and Neumann; but these observers hesitate to declare it the specific cause of the disease. The virus, whatever it may be, seems to be thrown off from the air-passages and conveyed perhaps by the breath, certainly by the sputum. That it is highly infectious, especially in the earlier period of the illness, there can be no doubt; and facts actually observed have shown that it can be conveyed from house to house by clothing. In all probability it is the sputum, far more than the breath, which serves as the medium by which infection is conveyed. If means be taken to disinfect the secretion from the air-passages, or to prevent it from coming into contact with healthy children, the latter, although living in the same house with the sufferer, will probably escape the disease. It has been noticed in the East London Hospital for Children that whooping-cough, when admitted accidentally into the wards, but rarely spreads to the beds around.

The susceptibility of a child to the complaint varies according to his age and physical state. Babies and the younger children take it most readily, so that it is far more common before the sixth or seventh year than at a later age. Strumous subjects are more susceptible to it than children of stronger constitution; and the state of physical depression left by certain diseases—by measles in particular—seems to prepare the child for ready infection by the whooping-cough virus. Epidemics are more common in the spring and autumn than at other seasons; and it is at these times that the greater proportion of deaths occur, for sudden changes in atmospheric conditions, by increasing the pulmonary catarrh, add to the intensity of the disease.

The period of **incubation** is not absolutely fixed; probably it varies in different individuals. In one very clear case noted by Dr. Bristowe the period was exactly a fortnight; but according to some writers it may be as short as four days. The infectiousness of the complaint begins with the earliest symptoms. It is, indeed, in this the early non-spasmodic stage that the child is most likely to be a source of danger to others; for when the whoop appears his power of communicating the disease begins to decline. Still it is not at an end until a period of at least six weeks has elapsed from the beginning of the attack.

Morbid Anatomy and Pathology.—In cases of death during an attack of pertussis the principal lesions depend upon the complication which has determined the fatal issue. In the uncomplicated complaint we find only congestion with hypersecretion of the mucous membrane lining the trachea and bronchi; a certain amount of emphysema and collapse of lung, due to the violence of the cough and spasm, and swelling of the bronchial glands. Von Herff, from laryngoscopic observations made upon himself during an attack, found that in the early stage there were traces only of catarrh in the pharynx, larynx and trachea; but that in the convulsive stage the catarrhal inflammation had spread to the lower surface of the epiglottis and to the mucous membrane of the arytenoid cartilages and of the cartilages of Santorini and Wrisberg. In the paroxysm the mucous membrane became dark red and covered with transparent mucus; and he always noticed a yellowish pellet of mucus, the size of a pea, on the posterior wall of the larynx.

The exact nature of whooping-cough is far from clear. That the disease is a general one, of which the catarrhal and nervous symptoms are the direct manifestation, can hardly be doubted. The virus affects in particular the pulmonary mucous membrane; and the peculiar spasmodic cough and whoop are usually referred to the action of the poison upon the peripheral ends of the pneumogastric nerve. But inhibition of the pneumogastric does not explain fully all the phenomena of the disease. There are cases, no doubt, where laryngeal spasm may be due to local irritation, for in the child any violent cough, such as that set up by the entrance of food or liquid into the larynx, may be followed by a whoop; indeed, in some children it seems likely that a non-infectious spasmodic cough may be due to exceptional sensitiveness of the mucous membrane in and about the glottis: but in the real whooping-cough the nervous element is not limited to a mere laryngeal spasm. The excitability of the child, and the curious state of nervous unrest in which he remains throughout the attack, are noticeable features of the illness; and the paroxysms are marked by a general agitation, muscular as well as nervous, which is peculiar and characteristic. This general agitation may find expression in convulsive attacks which leave no ill consequences behind, or in a state allied to tetany. The vomiting, too, although sometimes perhaps a reflex act, may also be an instance of the general nervous commotion. That it is not a necessary consequence of laryngeal irritation and spasm is shown in the case of the violent cough of enlarged bronchial glands which is not followed by retching and sickness. Moreover, in whooping-cough vomiting does not always find its place at the end of the fit of coughing; sometimes it occurs at the beginning, and is the first sign of the coming paroxysm. This curious fact seems to show that, in such cases at any rate, vomiting is the result not of mere local irritation but of the general nervous effervescence which is so characteristic of the disease.

Symptoms.—The early symptoms are merely those of an ordinary cold in the chest; and the slight elevation of temperature (which often stands at 100° or 101° F. in the evening) is that common to the beginning of a mild catarrh. As in ordinary chills, the gastric mucous membrane may participate in the derangement, so that the patient is dull and languid, eats nothing, and is inclined to lie about. This state of things may go on for a few days or several weeks, the cough growing more and more troublesome, especially at night. Examination of the chest detects nothing at first; later there may be a little dry rhonchus here and there about the back. The greater frequency of the cough at night should excite some suspicion. In the day the cough may seem of little importance; but after bed-time it is heard much more often, and is then apt to assume a convulsive character which is quite absent from it during the waking hours. It may be preceded or followed by violent sneezing and the discharge of quantities of thick mucus from the nose.

After a time the spasmodic stage begins, and puts an end at once to any uncertainty as to the nature of the child's complaint. The peculiar cough of pertussis is too well known to need description. It bursts out with boisterous violence in a quick succession of short, sharp hacks which drain the chest of air, and allow of no inspiratory relief. When the dull, reddish purple tint of the child's face shows that the supply of air is almost exhausted, the inspiratory muscles come into play, and air is drawn into the chest with the characteristic crowing sound. The paroxysm may now be at an end for the time, but in bad cases the lungs are no sooner refilled than the cough begins again; and again the child's face swells and reddens, and grows more and more dusky until, when he seems at his last gasp, the spasm once more partially relaxes and a new supply of air is taken in. In this way all the distressing phenomena of the attack may be repeated, perhaps several times, before the child—wet with perspiration and quite worn out—sinks back with livid lips and dark swollen eyelids in his nurse's arms. If an infant, the patient sleeps heavily after the attack is over. An older child may return to his play, but often complains of headache.

At the end of the fit of coughing the patient generally vomits, and sometimes he has also an involuntary action of the bowels. The former symptom is of some moment, for, if the vomiting be frequently repeated, it may make the work of nourishing the child a very anxious and difficult one. The ejected matters consist of the food taken mixed with large quantities of thick, ropy mucus. This mucus comes in part from the lungs, but in part it comes from the stomach; for a copious flux from the stomach and bowels is a common feature of the complaint.

One peculiarity of the cough is the child's evident anxiety to stave it off. His face all at once takes on a hard, set expression, with fixed eyes and compressed lips; then, as the desire to cough becomes more and more difficult to restrain, his cheeks grow red, his brows contract, and his forehead gets moist. Often, as the cough bursts out, there is a curious exhibition of nervous distress. The child may clutch his mother's neck as if in fear, or shiver as if with cold, or stamp with his feet upon the ground as if in a fit of rage.

During the access the pulse becomes very rapid, and sometimes can hardly be counted. Examination at the back of the chest at this time discovers nothing but wheezing sounds so long as the cough lasts, while in the long crowing inspiration all sounds are lost in the noise of the whoop. Between the attacks, if there be no pulmonary complications, the percussion note is slightly hyper-resonant, and scanty sonoro-sibilant rhonchus, with an occasional coarse bubble at the bases of the lungs, is all that can be heard with the stethoscope. In a doubtful case the marked contrast between the insignificance of the physical signs and the frequency and violence of the cough is by no means without its value in diagnosis.

In some children, who have a disposition to hernia, the strain of the cough may cause rupture; and the intense congestion which is always induced when the cough is prolonged often ends in hæmorrhage. Little cracks in the lips and gums invariably bleed, and in many cases there is hæmorrhage from the nose, the eyes, the mouth, and even the ears. Blood from the mouth comes, as a rule, from the posterior nares, very rarely from the lungs. If the paroxysms be frequent and the cough violent, the face may remain congested in the interval of the attacks. The eyes are injected and bloodshot, the lids discoloured and swollen, and the cheeks and lips a dusky red. In these cases it is common to find signs of subcutaneous extravasation. There may be ecchymosis of the conjunctiva, and small hæmorrhages in the thickened lids; or if the strain have been unusually severe, the eyelids may be mottled purple, green, and yellow, and the sclerotics stained blood red with the exception of a narrow white circle round the cornea.

There is one symptom, occasionally present at this time, which is very characteristic of the complaint; this is a sublingual ulceration. The sore is seated at the frænum of the tongue, and may reach for a little distance on each side of the middle line. The ulcer is only seen in infants at the beginning of dentition, when no teeth but the two central incisors have been cut in the lower jaw, and is due to the scraping of these teeth against the frænum as the tongue is protruded and withdrawn during the strain of coughing. It is never seen before the beginning of the spasmodic stage.

The number of the paroxysms and the frequency of their return vary partly with the severity of the attack, and partly with the degree of judgment shown in the management of the patient. Quiet, rest, and pastimes which amuse the child without exciting him, help to reduce the number and diminish the violence of the seizures, while emotional or other disturbances bring on his cough and increase the worry of his nervous system. The recumbent position, too, seems to favour the return of the cough, and currents of air passing across his face, especially during sleep, are apt to excite it at once.

In different cases and, indeed, in different epidemics there is great variety in the severity of the spasms. Some children only whoop occasionally; others whoop incessantly and with violence. Young infants whoop seldom, often not at all. As a rule, the coughing fits are longer at the beginning of the spasmodic stage than towards its end; and the diminution in the violence of the cough may be noticed to coincide with an increase in the quantity and tenacity of the mucous discharge. In ordinary cases the spasmodic stage lasts about a fortnight. Towards the end of this stage the whoop only accompanies the more violent fits of coughing, and is noticed with less and less frequency until it ceases altogether. The complaint has then passed into the stage of decline, and if ordinary prudence be shown by the child's attendants convalescence quickly follows. The whole time occupied by the attack varies from two weeks to eight or even ten; but the child is probably not infectious after the sixth week. In all cases where the disease is protracted beyond the normal period search must be made for adenoid growths in the nasopharynx. It is my experience that the irritation set up by these vegetations is often the cause of persistence in the cough and spasm after the whooping-cough proper is at an end.

Complications.—In the course of whooping-cough many complications may arise. Gastric disturbances and bowel complaints may give trouble, serious nervous symptoms are not uncommon, and various secondary disorders may attack the lungs and put the child's life at once into danger.

Disturbances of the stomach and bowels are the commonest of complications. The vomiting, if it be kept within due bounds, is of little importance; but if it take place with each access of cough, and this be frequently repeated, the difficulty of supplying the patient with sufficient nourishment becomes a serious one. This difficulty is increased by the copious mucous secretion which lines the walls of the stomach and interferes greatly with the digestion of the food retained. In such a state little chills are dangerous, for diarrhœa is easily excited; indeed, a certain looseness of the bowels, with the passage of slimy stools containing much mucus, and sometimes worms, is a common symptom of the disease. As a rule, intercurrent looseness of the bowels is not serious, but in hot weather a very severe watery diarrhœa may come on. This, while it lasts, may suppress all laryngeal and pulmonary symptoms, as Dr. R. J. Lee has pointed out, so that the presence of whooping-cough may not even be suspected.

In neurotic children a marked rise in temperature often accompanies the development of any gastric derangement. In uncomplicated whooping-cough the temperature is not elevated, at any rate after the first few days, so that any increase in the bodily heat may be taken as a sign of the presence of some disturbing element. This, however, is not necessarily of a dangerous character, even if the temperature reach 104° or 105° F. Such a heat with headache and nausea, perhaps vague bodily pains and loose unhealthy motions, may often be quickly relieved by a dose of castor oil.

Nervous accidents are common. Almost invariably in the course of the disease the child is noticed to be excitable and timorous, curiously impressionable, and easily startled. In such a state the occurrence of a nervous complication is not to be wondered at. In young children under two years of age we often find exaggeration of the laryngeal spasm. At the end of the fit of coughing the expected whoop is delayed, and the child remains with open mouth, staring eyes, and haggard dusky face, making agitated movements with his arms until a partial relaxation of the glottis allows a certain amount of air to penetrate into his lungs. This complication is in any case a dangerous one; but if it be combined with inflammatory mischief within the chest the danger is great indeed. Sometimes the spasm is followed by a state of more or less complete syncope or by a passing loss of vision. Severe headache is not uncommon after a paroxysm, and, according to Troitsky, there may be temporary deafness.

The exalted nervous sensibility, especially if combined with an imperfectly oxygenated state of the blood, may be a cause of general convulsions. Convulsions occurring in the course of whooping-cough, although necessarily an alarming symptom, are not always dangerous. Cases sometimes occur in which highly neurotic children, the subjects of pertussis, are seized with convulsions, and on these passing off seem none the worse for the accident. Some of these children may be slightly rickety, but this is not always the case. There can be no doubt that in whooping-cough, as in rickets, there is a heightened nervous impressionability, and that in such a state even slight worries may upset the balance of the nervous system. Unfortunately these harmless seizures are the exception, and not the rule. In most cases an eclamptic attack in the course of whooping-cough announces the onset of some dangerous complication. In this way convulsions may be the earliest symptom of embolism of cerebral vessels, of cerebral hæmorrhage, of thrombosis of intracranial sinuses, of diffuse collapse of the lung, or of broncho-pneumonia.

Violent and repeated convulsions may have dangerous consequences, however trifling the cause which has set them up. During the convulsive attack the strain upon the blood-vessels, as shown by the turgid state of the superficial veins of the face and neck, must be very severe. If this be prolonged or frequently repeated, as must happen during a series of such attacks, cerebral hæmorrhage, with more or less extensive paralysis, may ensue. Or, again, cerebral hæmorrhage, directly induced by the violence of the access of cough, may precede the convulsions and be the immediate cause of them. In all cases of the kind which have come under my notice the patient has been deeply cyanosed during the paroxysm of cough. The symptoms are those ordinarily attendant upon intracranial hæmorrhage, and the paralysis may be permanent with wasting of muscles and rigidity of joints. In other cases complete recovery takes place, and sometimes the improvement is so rapid that it is difficult to believe that the symptoms could have been due to a blood-clot in the brain.

Many varieties of nerve lesion may occur in the course of whooping-cough, and their pathology is often obscure. Troitsky, in an interesting paper on this subject, speaks of—(i.) Hemiplegia or a more limited paralysis; (ii.) a form of psychical blindness; (iii.) weakness and difficulty in walking; (iv.) transitory paralysis in all the limbs; (v.) loss or diminution of sensibility. Moebius, also, has recorded a case of pertussis complicated by ascending paralysis in a child of three. The weakness came on towards the end of the illness, and affected first the legs; then, as these improved, the arms; afterwards the muscles of the neck; and finally the diaphragm, so that respiration was conducted entirely by the abdominal and intercostal muscles. In the parts affected the reflexes were lost, but sensibility was preserved, and the electrical excitability was normal. There was no atrophy of muscle or affection of the bladder or rectum. The case ended in rapid and complete recovery, and Moebius attributed the symptoms to a multiple neuritis. Cases have also been published by Surmay, Sparks, and others, in which nervous symptoms preceding the whooping-cough were much intensified by the attack.

Aphasia sometimes occurs, and is usually combined with hemiplegia; but Troitsky refers to one case in which there were no definite symptoms of paralysis, and to others in which these were ill defined. The condition, in fact, might be compared to that met with sometimes at the end of enteric fever.

Some years ago I saw with Mr. Julius Cæsar a child, of two years old, who, after convulsions during an attack of pertussis, was left hemiplegic and with a curiously clouded state of the intellect. Two months after the attack the paralysis was still almost complete and the muscles flaccid, and the child lay in an apparently unconscious state with eyelids partially closed and sluggish pupils. Four months later the paralysis had disappeared, but intelligence did not return completely for some weeks longer. In the end recovery was perfect.

The pulmonary lesions form a very important group of complications, as it is to these accidents that death may usually be attributed. One of the most common of these is collapse of the lung. In every case where the patient is very young and the spasm violent, pulmonary collapse is to be feared, for all the conditions which favour the lesion are present at the same time. At the end of every prolonged paroxysmal cough the lungs are almost exhausted of their air, the thick mucus in the tubes offers an obstacle to their re-expansion, and the consequent state of muscular and nervous exhaustion seriously weakens the inspiratory power. A healthy infant, however, may still continue to carry on the respiratory function sufficiently, although not without effort; but if the child be the subject of rickets, reinflation of lung under such conditions and with softened ribs is often impossible. In young infants, if the pulmonary collapse be extensive, its occurrence is often indicated by a convulsive fit; or even, if the area affected be a very large one, by sudden death. In ordinary cases, where the collapsed area is of more moderate extent, the infant becomes suddenly still and cold: his face is dull white, his lips and eyelids are purple, his breathing is rapid and very shallow, and his nares act. The skin is often clammy and moist, and the internal temperature is low. The child can only be fed with difficulty, for he is unwilling or unable to swallow. He may die suddenly from syncope, or slowly from gradual extension of the collapsed area. Often the end is preceded by a convulsive fit.

In children beyond infancy the effect of pulmonary collapse is less severe. The patient is stronger, and, moreover, a smaller area of lung tissue is involved. The younger the child the greater the depression and the more pronounced the signs of deficient aeration of the blood; but at any age the complication is one to be regarded with some anxiety.

While in infants collapse of the lung is the common complication, in children of eighteen months and upwards bronchitis and catarrhal pneumonia are the chief intercurrent lesions. These, no doubt, are the consequence of a chill which causes extension of catarrh to the smaller tubes and alveoli of the lung. As long as the bronchitis is comparatively mild the whoop continues, and the symptoms generally, with the exception of a moderate rise of temperature, remain much as before. In a severe bronchitis, however, the whoop is suppressed, and all the symptoms of grave pulmonary catarrh immediately manifest themselves. If broncho-pneumonia supervene it is apt to occur in the subacute form; and, although necessarily a dangerous complication, may end favourably in a child of fairly good constitution. In the pneumonia the whoop is generally suppressed, but it may happen that laryngeal spasm, with or without a modified whoop, persists in the fits of coughing in spite of the occurrence of the complication. This, it is needless to say, adds greatly to the danger of the case.

Although catarrhal pneumonia is the common form of inflammation of the lung met with in pertussis, croupous pneumonia may occur. Its onset is often accompanied by violent and perhaps repeated convulsions; but the course of this form of pneumonia is comparatively brief, so that, although the patient may seem for a time to be in extreme danger, recovery is by no means impossible.

The pulmonary emphysema, which is almost invariably present in the upper lobes and anterior borders of the lungs, is of little moment; even if the smaller tubes participate in the dilatation. The condition is probably but a temporary one, and may be expected to subside after convalescence has been established. It may happen, however, that in an access of very violent cough an over-distended air-cell may rupture, and air be extravasated into the subpleural tissue: thence it may make its way, by the areolar tissue of the anterior mediastinum and beneath the deeper cervical fascia, to the subcutaneous tissue of the neck, the chest, the arms, the face, and even the eyelids. All these external parts are swollen, soft to the touch, and on pressure give the crepitating sensation so characteristic of surgical emphysema.

Acute parenchymatous nephritis is an occasional complication of whooping-cough, and according to Dr. Stefano Mircoli has been known to occur in no less than 12 per cent of the cases. This observer attributes the lesion to venous stasis caused by the obstruction of the vena cava through the violent paroxysms of coughing.

Sequels.—There are certain consequences of pertussis which may give trouble after the disease itself is over. In children who inherit a diathetic taint the dormant tendency may at once be roused into activity. Strumous children may begin to suffer from glandular enlargements and chronic discharges from which previously they had been free. Acute general tuberculosis may occur, as a consequence either of an inherited disposition suddenly waked to life, or of the softening of caseous glands; and syphilis may for the first time give signs of its presence in the system. Enlarged bronchial glands are a common consequence of an attack of whooping-cough, and chronic pulmonary diseases—such as chronic bronchitis with emphysema, asthma, chronic interstitial pneumonia, and pulmonary phthisis—not seldom owe their origin to this source.

The nervous excitability, so characteristic of pertussis, does not always subside when the disease itself comes to an end. Young children may suffer from laryngismus, the laryngeal spasm persisting and recurring irregularly without cough. In most of these cases adenoid vegetations will be found in the naso-pharynx. Older children may be left unusually timid, spiritless, and disposed to groundless alarms. They cry without reason, and are peevish and fretful at the merest trifle. Generally they are afraid of the dark, and even in daylight can hardly bear to be left alone. These signs of an unsettled nervous system may go on for months, although in other respects the child seems perfectly well. Often, however, the symptoms are kept up or even made worse, by a gastro-intestinal derangement which I have elsewhere described under the name of "mucous disease" (11).

Pertussis is so especially a complaint of childhood that its occurrence in adult life, if not very uncommon, is always unexpected. It may, however, be met with at any age, and is invariably a tedious malady, harassing alike to the sufferer and to his medical attendant. In its main features the disease is the same whatever the age of the patient; but after the period of childhood complications are rare. There is the same violence of cough, and the nervous agitation during the paroxysm is often very evident; but the spasm is less energetic, and gives way more easily, so that the whoop is not often heard. Vomiting, too, is less common, although sometimes the patient may retch at the end of the fit of coughing. The chief complaint is of disturbed rest at night, owing to the violence and frequency of the paroxysms.

Diagnosis.—In the early period of the attack it is not easy to distinguish between pertussis and ordinary tracheitis or a pulmonary catarrh. The whoop is not a constant feature of the illness: it is not heard until the cough is fully developed, and, indeed, in many cases is never heard at all. Moreover, in the child laryngeal irritation may set up a certain amount of spasm, so that a crowing inspiration at the end of a cough must not always be taken to imply that the complaint is pertussis. Again, vomiting is not a test symptom, for it is as often absent as present. Our diagnosis must rest, therefore, upon the general characters of the cough itself, especially upon its gradual development, and not upon the presence or absence of one or two accidental phenomena. The cough at the first is mild enough, but as the days pass it gets more and more frequent and less and less easy to control. The most striking feature is its suddenness. It bursts out and cannot be restrained; and as it goes on the cheeks and eyelids grow more and more congested and red. If a child be said to cough until he is red in the face we should always think of this complaint. Again, an early sign of pertussis is the frequency of the cough at night. If a child coughs much more in the night than he does in the day, it is to pertussis that our thoughts would naturally turn. The night cough, too, is often more characteristic than that which is heard while the child is up and about. The mother should therefore be directed to notice if at night the cough be prolonged or convulsive in character, and if the child seem at all exhausted by it, or have difficulty in getting his breath. Another fact, which in an uncomplicated case should open our eyes to the real nature of the complaint, is the trifling character of the physical signs. We hear that the patient's cough is incessant and distressing, and that at night his rest is continually broken by the frequent return of the paroxysms, but on examination of his chest we can find no more than a little sibilant rhonchus here and there about his back. This absence of physical signs is a very characteristic feature. In catarrhal pneumonia the cough may be violent and prolonged, but the physical signs show the pulmonary lesion, while the history and general symptoms of the case exclude whooping-cough as its cause. So also when the bronchial glands are enlarged the cough may be spasmodic and occur in paroxysms, but the general symptoms and signs of pressure prevent the condition being confounded with whooping-cough.

If convulsions occur it is very important to decide whether they depend upon the general nervous irritability or are symptomatic of some serious complication. In the latter case, if the complication be an attack of acute bronchitis or pneumonia the temperature becomes febrile, and the special physical signs will be discovered in the chest; at the same time the spasmodic character of the cough becomes very much modified. If collapse of the lung have occurred, the signs and symptoms proper to that lesion may be detected. So also if the complication be a cerebral one, evidence of the lesion will be quickly forthcoming. If the convulsion arise in a neurotic child from gastric disturbance acting upon a nervous system rendered by the complaint exceptionally sensitive to external impressions, or if it be due to partial asphyxia in a highly nervous subject, the eclamptic attack follows immediately upon the cough, and passes off quickly, leaving no ill consequences behind. Squinting, drowsiness or stupor left after the fit are especially dangerous symptoms, as they may betoken the occurrence of thrombosis of intracranial sinuses.

Prognosis.—The mortality of whooping-cough is high, but far higher than it need be. The chief dangers of the complaint arise from the occurrence of convulsions, of bronchitis with collapse, and of catarrhal pneumonia; but with proper care in the management of the child these dangers may for the most part be avoided. It is true that if the patient be an infant with softened ribs from rickets, the danger of collapse is really great; and it may be quite out of our power to avert a fatal issue. In ordinary cases, however, judicious precautions will carry the child safely through the attack: for, as a rule, when children die in pertussis they die from a perfectly avoidable complication; and this complication too often takes the shape of an inflammatory chest affection directly induced by sending the child out of doors into the cold. As a rule, so long as the disease remains simple the prognosis is favourable; but there are certain conditions which may place the patient at a disadvantage, and these must not be overlooked when we are estimating the chances of recovery. Thus in very young babies collapse of the lung is easily induced, and on this account pertussis during the first months of life is always to be regarded with anxiety. Again, a highly neurotic temperament is not a favourable preparation for a complaint which has a directly disturbing influence upon the nervous system; and these cases, too, demand especial care in their management. The course of whooping-cough is also affected by the presence of adenoid growths in the nasopharynx. The irritation set up by these vegetations may be sufficient greatly to increase the intensity of the spasm, and probably also to maintain the nervous element in the cough for weeks together. Most of the cases of protracted whooping-cough, or of apparent relapse after recovery, are met with in children who are troubled with these vegetations.

The occurrence of any complication adds much to the gravity of the case. Great agitation and excitement on the approach of the access of cough, or extreme cyanosis during its course, make us fear the onset of convulsions. Should an eclamptic attack occur, we scan very narrowly the condition in which the patient is left when the fit is at an end. If he seem contented and cheerful there is so far no cause for anxiety; but if he be drowsy and stupid, or show any special sign of cerebral lesion, or if he lie pale and still with active nares and quick shallow breathing from collapse of lung, death is almost certain. Convulsions which usher in a pneumonic complication, even although repeated and violent, are rarely immediately fatal, and if the lung inflammation be of moderate extent, the case may still end favourably. Laryngismus stridulus, with extensive broncho-pneumonia or serious bronchitis in a rickety subject, offers small prospects of recovery.

Treatment.—In order to guide a case of whooping-cough to a favourable issue we must do our best, while promoting the healthy nutrition of the patient, to ward off the complications to which the chief mortality of the disease is due. We must remember that the mucous membranes are already in a state of catarrh, and therefore highly susceptible to changes of temperature, and that to send the patient daily out of doors, with little regard to the state of the weather (as is so often done), is hardly the way to keep his chest free from grave intercurrent disease.

The best way to shorten the attack and prevent the onset of complications is to confine the patient strictly to two rooms, and to keep him both by day and night in a properly medicated atmosphere. The temperature of the rooms should be maintained as nearly as possible at 65°; and if the rooms do not communicate, the child must be carried from one to the other wrapped from head to foot in a blanket. The air can be medicated in various ways. Creosote or eucalyptus oil may be volatilised from a metal saucer placed over a spirit lamp; a solution of carbolic acid (one part in thirty of water) may be vaporised by means of Dr. R. J. Lee's "steam draft inhaler"; or sulphurous acid may be diffused through the room by burning small sulphur pastilles at short intervals. In children who are old enough to follow directions other topical remedies may be used in addition. Thus a 2 per cent solution of salicylic acid or resorcin may be sprayed for one minute into the child's throat every two or three hours while he inspires deeply. The spray is far more useful than the brush for applying remedies in this complaint. The latter usually excites the utmost alarm and annoyance; indeed, the mere sight of it is enough with most children to bring on a paroxysm at once.

While the fever lasts the patient should be kept in bed: afterwards he may be allowed to dress, but must still remain in the medicated atmosphere, at any rate until the spasmodic stage has come to an end. When he leaves a room the windows and doors should at once be thrown open so that the fresh air can enter freely until the time comes to warm and medicate the room again for the child's return. By this means the disease is treated topically, while complications—at any rate such as arise from chill—are guarded against. To diminish still further the risk of cold it is well for a time to forbid a bath, or, indeed, any washing of the child's body; for few children with whooping-cough can be submitted without danger to the exposure involved in an ordinary nursery bath. The dress should be warm, especially over the chest, and it is advisable to keep this part covered with a layer of cotton wool. The child must be amused with unexciting games, and it is better not to tease him with lessons, at any rate until convalescence is well advanced. In regulating his diet, foods which promote fermentation and acidity, such as potatoes, farinaceous puddings, jams, and fruit, are better avoided. These things make the child flatulent and uneasy, disturb his rest at night, and increase the fluster of his nerves.

In addition to the topical treatment internal remedies should be given to allay nervous irritation and reduce spasm. The drug upon which above all others I am wont to rely is the croton chloral hydrate given in doses of one grain every two, three, four, or six hours, according to the age of the child. It may be usefully combined with double the quantity of bromide of potassium. Another favourite remedy is the sulphate of zinc in doses of one-sixth of a grain (for a child twelve months old) given with half a drop of liq. atropiæ (B.P.) twice a day for three days; then every six hours for three days longer; afterwards with increasing frequency until slight dilatation of the pupil is noticed. It is advisable to keep the pupil thus dilated for at least a week. Antipyrin is preferred by some practitioners; it is given, in doses of one grain for every year of the child's life, every four, six, or eight hours. All these remedies have a very decided influence in reducing the spasm and shortening the attack, and will be found quite sufficient by most practical men. Many others may, however, be given; indeed, the whole list of antispasmodics and sedatives is open to the prescriber if he wish for variety. This class of remedy is to be resorted to directly the complaint is recognised as whooping-cough, and is of especial value at an early period of the illness. As we approach the end of the spasmodic stage there are two other drugs which have great value if the spasm be slow to yield. These are quinine in full doses, and the liquid extract of grindelia. Of the former one grain may be given, with one of antipyrin, twice a day to a child of one year old, and one grain of each may be added for every year of the child's life, until a dose of five grains is reached. The quantity of the grindelia extract to be given to an infant is ten drops every four hours. Either of these will usually make an immediate impression upon the complaint. At the same time it must be remembered that obstinate cases are mostly met with in children who are troubled with naso-pharyngeal vegetations. Search, therefore, should be made for adenoid growths, so that, if present, they may be removed without delay. Counter-irritation of the chest is usually advised, and is greatly relied upon as a domestic remedy. It is no doubt of service if pulmonary catarrh be well marked, or there be a tendency to collapse of lung.

Any complication which may occur should receive early attention. Excessive vomiting may be controlled by small doses of cocaine (one-sixth of a grain twice a day to a child of one year old). Looseness of the bowels quickly yields to a dose of castor-oil. Excess of spasm or unwonted nervous excitement may often be checked by chloral and the bromides; and immediate relaxation of the glottis usually follows dipping the child's hands into cold water. Convulsions and the pulmonary complications must receive early treatment, and any temporary weakness or tendency to syncope must be combated by free stimulation. During convalescence a change to a dry bracing air is of great advantage in calming nervous excitement and restoring strength.

Eustace Smith.

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E. S.

CONSTITUTIONAL SYPHILIS

The specific fever known as Syphilis differs chiefly from its congeners in the much more prolonged duration of its several stages. Like small-pox, measles, scarlet fever, and the others in this group, it is communicable from the diseased to the healthy, and can be produced by no other means. Like them it has its several stages of incubation, efflorescence, relapse, decline, and sequel. As in them, so in syphilis, the most prominent symptom is an exanthem or cutaneous rash. The various stages of syphilis tend to pass away of themselves, in the course of time, almost as certainly as do those of small-pox; and one attack affords for a time immunity from a second. As is the case in the other zymotic diseases, the poison of syphilis is one which possesses the power of breeding in the patient's body; and the smallest possible quantity of virus suffices in due time to infect all the solids and fluids of the system. The time required, however, is much longer, and the stages are much more protracted. Instead of counting the duration of its stages by days, we have to count by weeks, or by months. From this circumstance there follow, in the most natural manner, certain apparent differences between syphilis and the other fevers. Thus, because the evolution of the exanthem is slow and gradual, the pyrexial disturbance attending it rarely rises to any great height; and because each stage is so much longer, correspondingly wider margins for occasional variation in length must be allowed. It further follows that as the disease extends over years, and its subjects may not be incapacitated by it for social life, many, whilst still infected, become parents, and transmit their taint to their offspring; a circumstance which can but very rarely happen in the more short-lived and acute fevers.[1] These apparent differences are by no means real ones. And it is probably by no means correct to allege that syphilis is the only fever which has a tertiary stage. What are called the tertiary symptoms of syphilis find their analogues in many cases of small-pox or scarlet fever, in what are known as the sequels of those diseases; it is true that these occur only in a small proportion of cases, but the same holds good of the tertiary syphilitic phenomena. If we observed more carefully, it is probable that the sequels of the exanthems might be recognised much more often than they now are; and that many of the diseases classed as "strumous"—inflammations of the eye, the ear, or the skin, or again some diseases of bones and joints—are, at any rate in part, the tertiary consequences of some specific fever. So, too, if it be alleged that the stages of syphilis may be shortened and otherwise modified by treatment, whilst those of the other exanthems cannot, we may reply that those of the latter are too short and transitory to give time for a fair trial of remedies; and further, that it is by no means proved that mercury given with sufficient vigour and promptitude would have no influence over such a disease as small-pox. Syphilis does, fortunately, differ from most of the other specific fevers, in that its virus is incapable of diffusion in the atmosphere, and that consequently it is contagious only, and not infectious also; but it is by no means solitary in this feature.

Having thus defined the rank which true syphilis ought to occupy in our nosological classifications,—a point of the utmost importance to our correct appreciation of its nature,—we may next ask the question, whether under this name we have to deal with one disease or with several. Every surgeon is aware that there are many venereal sores which are not followed by syphilis, and very different opinions have been entertained of the relation which these hold to the real disease. Some have assumed, with Carmichael, that there are several distinct poisons; others hold that there are certainly two. Without entering at length into the controversy, I may remark that the evidence in favour either of *plurality or of duality*[2] has always been to my mind quite inconclusive. Let us accept clearly the doctrine—so essential to the explanation of numerous pathological phenomena—that all products of inflammation are contagious, and capable of producing disorders similar to those in which they have originated, and we shall not have much difficulty in explaining the different forms of non-syphilitic venereal sores. The majority of the latter are probably *abortive inoculations.* In the performance of vaccination the utmost care is taken to secure the true virus, yet not infrequently abortive sores are produced. If it were the practice to inoculate again from these abortive sores when suppurating, we might soon produce an analogous state of things to what we now have in respect to the soft and hard chancre. The communication of syphilis is, of course, a matter of mere chance, and the virus with which it is effected can be but very seldom in a state of purity. It is probable that very often the secretion which effects it does not contain the specific virus of syphilis in a form capable of its own reproduction. In other instances sores may result from inoculations of a mixed secretion containing the true virus, but with it an irritant capable of producing inflammatory action of a kind likely to be destructive to its vitality. A chancre which ulcerates quickly may very possibly thus rid itself of a virus which would otherwise have gone through its stage of incubation. Further, we must remember that this stage of the primary sore is transitory, and that those who have once had it but seldom have it again. A large proportion of the women by whom contagion is communicated have had syphilis long before, and are incapable of originating the true virus. The sores which they possess are analogous to those caused by vaccination in protected persons. Attention to these considerations would, I feel confident, enable us to put aside the unnecessary hypothesis of duality.[1]

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[1] Hereditary transmission occurs in all specific fevers if it chance that offspring is produced whilst the parent is suffering.

[2] Surely it is absurd to speak of the "duality" of things which have scarcely any features in common. The production of constitutional phenomena is the essential feature of syphilis, and as thus denoted there are not two forms of syphilis. We may freely admit that, in impure sexual intercourse, fluids of very various qualities and endowments may be inoculated, and thus very different kinds of local ulcers may result, but there is only one poison which can produce syphilis.

In a medical essay on syphilis any detailed consideration of the **primary symptoms** would be out of place. It may be sufficient to say that the success of a syphilitic inoculation is denoted by the formation of a base of induration beneath the abrasion first noticed; that this induration is seldom well characterised until three weeks or a month after the contagion; that it is usually attended by very little either of ulceration or suppuration, and that it causes an enlargement of the proximal lymphatic glands. The bubo shows the same tendencies as does the chancre. There is hardness, with but little swelling, and rarely much tendency to the formation of pus. These characters will usually be the same, or nearly the same, in both sexes, at all ages, and on all parts of the body. It must, however, be freely admitted that many chancres which infect are yet never indurated. Some writers hold that certain parts never exhibit the phenomenon of induration when inoculated. My own experience is, however, that chancres with well-characterised induration may be met with in most various positions; for example, in the glans penis, the nipple, the lips, the eyelids, the hands, and so on.

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[1] An attempt has recently been made to claim the Tropical disease Yaws as a malady, which, whilst distinct from syphilis, yet resembles it in having a primary sore, secondary eruption, and a tertiary stage; and to construct a family of "Syphiloids." After careful examination of the evidence, I entertain a strong suspicion that the phenomena of yaws are really those of syphilis, and that its supposed differences are due to race and climate. Its different stages are curable only by the specifics for syphilis. See an *Essay on Yaws* by Dr. Numa Rat, with a preface by myself; see also a Government Report by Dr. Nichols.

Secondary Symptoms.—A successful inoculation having been effected, a *period of incubation* now ensues which may last from one to three months, and usually averages about six weeks. During the latter part of this period the patient is often sensible of some malaise and discomfort, and may be feverish in the evening. At length an exanthem makes its appearance, affecting both the skin and the mucous membranes. The skin shows a scattered eruption, which may vary very considerably in some of its characters, but usually conforms to rule in being of a coppery hue, and in preferring the fronts of the limbs to their dorsal aspects. This rash may be merely congestive, resembling that of measles; or it may be scaly, papular, eczematous, pustular or bullous. In some few cases it is attended by ulceration, but as a rule it involves only the superficial layers of the skin, differing in this respect from the tertiary manifestations. There is not the slightest reason for believing that these differences in the character of the exanthem imply difference in the nature of the virus. Chancres exactly corresponding in their characters may be followed by most diverse kinds of eruption. Simultaneously with the eruption on the skin we usually observe evidences of similar implication of the mucous surfaces. In the tonsils symmetrical ulcers form; these ulcers are often of kidney-shape, and have a tawny, gray base with abrupt edges. They are attended by but little pain, and do not spread much either laterally or in depth. After lasting for a few weeks they usually heal. These tonsillar ulcers are rarely absent in the exanthematous stage. Very often, but not nearly so constantly, we observe also certain superficial patches of inflamed mucous membrane in the mouth; on the pharynx, palate, tongue or cheeks. On the tongue, and at the corners of the mouth, and sometimes in other positions also, these patches become very considerably raised, and assume the condition known as condylomas. If condylomas be observed in the pharynx, they will almost always be found at the anus also, and conversely. They are to be regarded as patches of cutaneous eruption modified by their position and by the moisture of the parts. Whether or not in these cases any eruption extends through the alimentary canal is a point upon which we have no evidence. That there is in this stage a tendency to overgrowth as well as to inflammatory changes is proved by the occasional production of well-characterised papilloma, especially on the tongue.

The exanthem usually takes from a fortnight to a month before it is fully out, and about two months are usually occupied in its gradual decline. In some cases it is very transitory; in some it is greatly prolonged. When it is at its height, or just when it begins to decline, it is not infrequent for inflammation of the iris to occur. The iritis, when it happens, is usually symmetrical. It is attended by the free effusion of lymph, often in elevated nodules of a salmon or rust tint; the characteristic zone of ciliary congestion is usually well marked, and there is often a dotted deposit in the posterior lamina of the cornea. In other cases, instead of iritis or coincident with it, inflammation of the retina occurs. The retinitis is, I think, usually a little later than the iritis, and we rarely see it until the eruption on the skin is disappearing. This form of retinitis is not uncommon, and is a very insidious and most important malady. The patient notices nothing, excepting that his sight is very dim; he has no pain, no congestion of the front of the eye, no intolerance of light. The ophthalmoscope shows us the retina hazy, and as if stained with port wine; the optic disc slightly swollen and its margins indistinct; and not infrequently numerous small extravasations of blood are seen.

It is currently supposed that syphilitic iritis may occur at almost any period in the course of the disease. I speak after close attention to this subject, when I assert that all our well-marked examples of this disease present themselves amongst the secondary phenomena. From three to six months after the chancre is the usual date. When once iritis has occurred, and adhesions have been left, relapses are liable to happen; and it is this fact which has led to the error which I am endeavouring to confute. In these relapsing cases, however, the symptoms are very different from those of the first attack. The infusion of lymph is much less free, no nodules are seen, and rarely are both eyes simultaneously affected.

Whilst the local phenomena just mentioned are occurring, there are usually present others of a less definite character. The patient loses flesh, he is restless and slightly feverish, the appetite is deficient, the bones and joints ache, and the hair becomes dry and thin. Now and then swellings occur on certain bones, more especially on those of the skull; but in this stage periostitis is always slight and transitory, and never leads to suppuration. At this stage also the patient may suddenly become deaf in one or both ears, and now and then facial paralysis attends the deafness.

Such are the various symptoms which mark what is called the secondary stage of syphilis. In many cases only a few of them occur, the rash on the skin and the ulcers in the tonsils being those which are most constant. In many individuals all the secondary symptoms have disappeared within six months of the original contagion; but in a larger number a year elapses before such is the case. It is rare for any symptoms belonging to the secondary group to linger after eighteen months have passed, although their effects are often seen much later. That these symptoms may disappear in a most satisfactory manner, quite irrespective of any treatment which may have been adopted, is a fact confirmed by every day's experience.

Tertiary Symptoms.—When the group of secondary symptoms has passed away there usually follows a period of apparent health, during which the patient believes himself wholly cured. The interval between the well-characterised secondary and the well-characterised tertiary symptoms is one of different degrees of immunity in different cases. In many persons, I think in the majority, the disease is wholly latent, and the patient experiences nothing whatever to remind him of his taint. In many others, however, recurrences of symptoms, which it is difficult to assign to either group, continue to show themselves. Superficial sores on the tongue or the mucous membrane of the mouth, isolated patches of scaly or desquamating eruption on the skin, especially psoriasis palmaris, are the most frequent of these. Sometimes they are symmetrical; at other times not so. Such symptoms may continue to recur for many years (even to twenty) after the contagion. They probably depend rather on permanent tissue-contamination than on still existing blood disease. At any rate I may safely assert that we never witness any true recurrence of the secondary epoch. The eruption is rarely very copious, and is rarely of such a character as to deceive an experienced eye; nor is it attended by the ulcers in the tonsils, or iritis, which are so common in the secondary stage. In rare instances, at an interval of perhaps a year or eighteen months after infection, a relapse of a general symmetrical rash may occur. This rash may assume the form of rupia, and be attended by severe constitutional symptoms.

Speaking generally, however, after an interval, which may vary in length from a few months to a few years after the cessation of secondary phenomena, symptoms of a different kind ensue. Inflammatory indurations of a chronic character, and tending slowly to softening and ulceration, occur in the deep-seated tissues, or in the deeper parts of the superficial ones. In this way the skin, the subcutaneous tissue, the periosteum, the muscles, the internal viscera, the organs of special sense, and even the cerebro-spinal system itself, may be attacked. A remarkable difference is to be observed between secondary and tertiary symptoms as regards the symmetry of the inflammations produced. In the secondary stage a tendency to symmetry, often very exact, is observed, proving that the producing cause is free in the blood, and is supplied impartially to both halves of the body. In the tertiary stage the lesions are often single, or, if multiple, they display but little accuracy of symmetrical arrangement. This fact implies that they result from disturbed organisation of the solids, rather than from any poison still existing in the circulating fluids. The occurrence of the tertiary symptoms is to be explained by the fact, that during the exanthematous-stage, when the whole blood was loaded with the virus, the various solids received the elements necessary for their growth from poisoned blood. Hence an impairment of organisation in such tissues, and a liability under slight exciting causes, or even in the ordinary course of nutritional change, to the occurrence of specific forms of inflammation. It is easy to see that in syphilis, with its very prolonged period of blood-poisoning, the risk of permanent tissue-modification must be much greater than in the other fevers, in which it is so short. During the exanthem stage of small-pox probably but little in the way of nutrition is effected; the changes being chiefly those of waste and disintegration. From this, it almost follows that the more prolonged and severe the secondary stage, the greater the risk of tertiary symptoms.

The following is a statement, in tabular form, of the various symptoms of the different stages of syphilis:—

1st Stage.—*Inoculation* and *Incubation.* Average duration, six weeks to two months.	An ulcer with indurated base and but very scanty secretion. Induration of the nearest lymphatic glands, with but little adjacent inflammation or tendency to suppurate.
2nd Stage.—*The Humoral* or *Exanthem*, that of secondary symptoms. Average duration, two to six months; may extend over a year, or even much longer. Lesions general, symmetrical, and not serpiginous.	Symmetrical ulcers in the tonsils, not spreading either in width or depth. A symmetrical eruption on the skin. Condylomatous patches on the mucous surfaces, and on the skin adjacent to the mucous orifices, usually symmetrical. Iritis, retinitis, or otitis; mostly symmetrical. Pains in bones and joints. Febrile disturbance. Loss of hair. Slight enlargement of lymphatic glands in all parts. Arteritis and other affections of the blood-vessels.
3rd Stage.—*Interval of latency or of relapses.* May vary from a few months to many years. Often persistently local.	In some cases the patient is wholly free from symptoms, but in a certain number reminders occur from time to time in the form of scattered scaly patches or rings, especially on scrotum, psoriasis palmaris, sores on the tongue, lips, etc. Recurring herpes on genitals, or in mouth.
4th Stage.—*Tertiary symptoms or sequels.* Of uncertain duration, and often characterised by a remarkable tendency to relapse. Lesions local, not symmetrical, and serpiginous.	Asymmetrical ulcerations in the mouth and throat, tending to spread widely and deeply. Asymmetrical lupoid ulcerations of the skin. Nodes of periosteum, cellular tissue, muscle, tendon, fascia, or nerve; not usually symmetrical, chronic in progress, tending to ulcerate or even to slough. Diseases of viscera, blood-vessels and nervous system.

Having thus sketched the normal course of syphilis in its several stages and its sequels, we must next consider the conditions under which its orderly evolution may be interfered with. These conditions are precisely the same as those which may disturb the course of any other exanthem. We have, 1st, idiosyncrasy; 2nd, the coexistence of some diathesis or of some other specific disease; 3rd, immunity, partial or complete, obtained by a previous attack of the same disease; 4th, inherited immunity, partial or complete; 5th, imperfect inoculation; 6th, the influence of treatment.

1st, To take first *idiosyncrasy*, I may simply remark that it is a matter of general experience that certain constitutions resist the specific animal poisons in a most remarkable manner. We are unable to offer any explanation of the fact; and, on the other hand, we meet with those who succumb easily and suffer severely. The influence of these inexplicable peculiarities in individuals is frequently observed in reference to syphilis.

2nd, The existence of some *special diathesis* or of some *other specific fever* at the time of syphilitic inoculation may modify the course of the latter. Possibly we overrate rather than otherwise the effects of these influences. Although it is not infrequent to find a delicate scrofulous subject suffering with unusual severity from syphilitic poisoning, yet the converse is almost equally common; we often see the delicate escape easily and the robust suffer very severely. There can be little doubt, however, that the tendency to suppuration and ulceration is much greater in those of fair skin and sanguine temperament than it is in others. The influence of diathesis (scrofula) is also often felt in preventing recourse to specific treatment. There is probably no reason to believe that the existence either of a diathesis or of another specific fever will materially modify the duration of the several stages of syphilis.

3rd, *A previous attack of the same disease* is well known to exert a most important influence upon the course of a second in the same individual. It is generally understood that syphilis, once had, is protective in the majority of cases against any second attack; and second attacks when they do occur are much modified. There is reason to believe that second inoculations are common, and that they usually end in the production only of the soft chancre (abortive sore). It is, however, quite certain that second infections of syphilis may be followed by the full phenomena of the disease.

4th, Of yet wider importance is the question of *the influence of disease in the parent in affording protection, partial or complete, to the offspring.* If we grant, as we must, the two postulates—firstly, that syphilis is transmissible to offspring; and, secondly, that it is protective for a certain time against second contagion—then we are obliged to admit that just as the disease itself may be transmitted, so may the immunity which it affords. Here again we have as yet very little clinical evidence on which to build; but what we do possess certainly favours the view that those who have suffered in infancy from inherited disease are to some extent protected.

Second infection usually results in the production of a much milder form of the disease. This is what occurs in cases of small-pox after vaccination; after a previous attack of the true disease; and indeed in second attacks of any of the specific fevers. It is surely impossible to believe that the constitution of a person who has passed through the stages of any of these diseases ever again returns into precisely the same condition in relation to the virus in question that it was before; and it is equally inconceivable but that some share of this peculiarity shall be transmitted to offspring. A child born of parents neither of whom is liable to small-pox or to syphilis, as the case may be, must be in a different position as regards those diseases from the child of parents both of whom are liable. Now, it is a matter of well-proven observation that any specific disease will be especially severe when imported into a community previously free from it. The ravages of small-pox in a virgin race is something far beyond what is ever known in a community long accustomed to the disease. There are also some reasons for believing that during the last two centuries syphilis has become a milder disease than it was when it first invaded Europe. This amelioration we may explain by recourse to the hypothesis above suggested;[1] but in doing so it must be borne in mind that improved treatment may have had its share.[2]

Lastly, we have to ask the all-important question, *whether the ordinary evolution of syphilis can be altered in any way by measures of treatment.* It will probably be admitted that physicians have abandoned the notion that it is practicable by medication to regulate in any way the course of the other exanthems. They are generally acknowledged to be diseases which always run their course. With the exception, perhaps, of cinchonism as a remedy for malarial fever, no single specific in the present day enjoys any repute for cutting short the course of these diseases. But we must not too hastily assume *a priori* that the same will hold true as to syphilis. It is possible that the stages of the other exanthems are too short to permit of the beneficial influence of antidotes. Few questions in therapeutics have been more hotly debated than the efficiency of certain drugs in syphilis. By some their specific power has been positively asserted, by others as strenuously denied. When, in 1866, I wrote for Reynolds' *System of Medicine* the article on syphilis upon which the present one is based, I recorded the opinion that it was not possible to prevent the secondary phenomena by mercury. During the years which have since elapsed, however, great progress has been made, and it is now justifiable to write that, if treatment be begun early and efficiently carried out, it is perfectly possible to suppress syphilis and to prevent the occurrence of any of the humoral group of symptoms. If mercury be begun as soon as the state of the sore permits of diagnosis, and continued without intermission in small but adequate doses, the patient will usually entirely escape both sore throat and eruption. A most interesting conclusive proof that the disease is really thus held under, as it were, by the drug is derived from the fact that if the latter be left off prematurely an eruption will make its appearance about six weeks later. Such eruptions are, however, always very mild, and yield at once when the remedy is resumed. It would appear that, in many cases, a year's administration of the remedy, without any intermissions, is necessary to the permanent suppression of the disease. For ten years past I have been practising this early and continuous method, and can speak definitely as to the uniformity of the results. The details of this treatment will come under consideration later; for the present I allude to the subject chiefly in order to emphasise the fact that we have in mercury a drug which is powerful to suppress the phenomena of syphilis and to change the course of their evolution. It is too soon to make any attempt to prove that patients so treated are less liable than others to tertiary affections, but so far my experience has been that they escape the class of phenomena grouped as "reminders" (the intermediate stage) and are to all appearance cured. It may not be out of place to remind the reader that under the older surgeons, who did not attempt any differential diagnosis of chancres, mercurial treatment was commenced indiscriminately at a very early stage. It is not improbable that in this somewhat haphazard manner they succeeded not infrequently in suppressing the disease entirely. They were, however, much exposed to risk of failure from their habit of giving large doses and very short courses.

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[1] This subject will be found very ably treated in Mr. Lee's *Lectures on Syphilis* (Lecture xi. page 209). I published in the *British Medical Journal* some cases in which patients who had suffered from inherited syphilis subsequently contracted venereal sores. These cases were, I believe, the first facts relating to the subject which had been recorded. Others had arrived at the same conclusions, but it was by *a priori* reasoning rather than by deduction from facts. Subsequently I published a case in which a patient who was the subject of inherited taint not only contracted a venereal sore, but experienced an outbreak of constitutional symptoms. I recorded a number of facts bearing on this subject in the second volume of the *London Hospital Reports*.

[2] If we reflect on the mode in which syphilitic inoculation is usually effected, the wonder will be, not that apparent varieties both in primary and secondary symptoms occur, but that the disease is so uniform as it undoubtedly is. Here, if anywhere, are the conditions under which we might expect a new species to originate. In the first place the virus is constantly mixed with other secretions, and very frequently with those of inflammatory origin. In a great many instances the person from whom the contagion is received is one whose own body has been previously rendered proof against the disease. Most prostitutes probably suffer from syphilis early in life, and during the greater part of the period during which they continue their vocation are incapable of being themselves again affected by true syphilis, although still liable to contract and to transmit primary sores of a modified character. Then, not only must we make allowance for differences in the kind of secretion with which the inoculation is effected, but also for differences in the recipient's state as regards it. Hence the differences in the cutaneous rash which follows—from a roseola to psoriasis and to rupia.

Modes of Communication.—Whilst the other exanthems are for the most part communicable only by direct contagion or infection to the individual concerned, syphilis, in consequence of its very protracted duration, may be conveyed in any one of four different modes. First, contagion direct to the individual; second, contagion indirect through the fœtus (possibly only in women); third, contagion from a mother who acquires syphilis during her pregnancy to a previously healthy fœtus; and, fourth, by sperm or germ transmission at the date of conception.

The period during which direct contagion is possible extends from the first appearance of the chancre to the end of the humoral or secondary stage. The primary sore is more actively contagious than are any in the secondary stage, but there can be no doubt that under favourable conditions the germs of the disease may be conveyed by the latter. When syphilis is communicated to a mother by contamination from the fluids of a fœtus with which she is pregnant, the course of the disease is materially different from what it is when received by other means. As a rule the woman shows no symptoms during her pregnancy, and may appear to be in perfect health. This may happen repeatedly, and throughout there may be nothing to disclose the fact that the maternal fluids have been in any way contaminated. That they do, however, invariably receive the taint, is proved by the fact that such mothers never (with the very rarest exceptions) contract chancres from nursing their infected infants (Colles' law). They are protected. In many cases, however, such mothers do subsequently suffer from definite maladies more or less closely resembling those of the tertiary class.[1]

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[1] I am aware that many cases have been published in which contamination from the fœtus was held to explain severe outbreaks of secondary syphilis. Without venturing

When syphilis is transmitted from parent to offspring various important peculiarities are observed in its manifestations. In the first place, the phenomena of the secondary and tertiary stages may seem to occur together; or at any rate we have a superficial rash on the skin resembling a secondary one, coincident with nodes on the bones and with deposits in the viscera. These cases are, however, exceptional; as a rule the stages occur as in the adult, the secondary rash disappearing after a few months, and a prolonged period of health intervening before the tertiary symptoms show themselves. It is possible when severe disease of the bones or viscera, or both, occurs in young infants simultaneously with skin eruptions, that we ought to regard such lesions as being merely very severe secondary phenomena. Unless fatal they are transitory and very different from the chronic affections of the true tertiary class to which the subjects of inherited taint are liable in after-years. The effect of the syphilitic poison upon the ovum is in many instances to destroy its vitality at an early period, and consequently to induce abortion. This, however, is far from being its constant effect. In the majority of such conceptions the tainted fœtus is carried to its full period. In exceptional instances it is then brought into the world with manifestations of its disease already apparent; more usually this is not so, and the infant, which when a few weeks old will suffer most severely, appears at first to be perfectly healthy. In these infants a period of from a fortnight to two months usually elapses, and then a rash appears, and the nostrils become stopped by swelling. At this stage the mouth is usually hot, its mucous membrane red and tumid, and the gums swollen. The child wastes, and assumes a shrivelled, senile aspect. Sometimes acute, well-characterised iritis occurs. Condylomas are frequently seen. The cutaneous exanthem may vary in character, much as we find it do in the adult. Many children die during this evolution of secondary symptoms. If they survive they usually in the course of a year get rid of all traces of disease, excepting perhaps an unusual pallor of skin, certain scars which may have been left on the face by the eruption, and an expanded nasal bridge caused by the long-continued swelling of the parts within.

I have said above that the tertiary and secondary stages sometimes appear to be strangely mixed in the early symptoms presented by syphilitic infants. Amongst the phenomena which we occasionally meet with under these circumstances are nodes of the skull and long bones, and gummas of cellular tissue, of tendon, or of muscle. The liver, kidneys, thymus gland, and other parts, may also be attacked. Such children are certainly more liable than others to serous inflammations. Serous

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to deny or even to doubt such a possibility, I may yet suggest that in many or all of these the primary sore had been overlooked. As regards the third mode we have no facts in proof that syphilis so acquired differs from that obtained by a fœtus at the date of conception. It is desirable, however, that we should keep in mind the possibility that there may be a difference. It is quite certain that a pregnant woman who acquires syphilis may and commonly does infect her fœtus, and that the infant born under such circumstances may suffer severely, and, I think, from the usual train of symptoms.

arachnitis to a slight extent is very common, and pleurisy is not an infrequent cause of death.

A condition of *severe anæmia* often results during the outbreak of early symptoms in a syphilitic infant, and from this death often results. In many cases, however, the child does not emaciate, but retains an appearance of good health which is remarkable, considering the nature of the disease. I have often seen infants who were well grown, stout and strong in an unusual degree, who yet presented well-characterised indications of inherited taint.

In the child as in the adult the secondary symptoms pass away in due time, and a period of health or latency ensues, of variable duration; after which the later phenomena show themselves. These are in part of the same character as those in the adult, but with the addition of several others which are not often met with in connection with the acquired disease. There are few more remarkable facts in the history of this most interesting malady than that the disease known as interstitial or syphilitic keratitis almost never occurs as a consequence of acquired disease; whilst it is common in the inherited form. I must also note here a remarkable exception to what I have stated to be the characteristic of tertiary symptoms in the adult, that they are but exceptionally symmetrical. It is a curiously difficult question to determine whether the late phenomena of inherited disease should rank as secondary or tertiary. Although it may seem almost absurd to claim inflammations as secondary which may occur thirty or forty years after birth, yet there are certain facts which strongly suggest that this would be the most correct method of arranging them. What we have hitherto counted as the tertiary symptoms in the inherited disease are very different from those of the acquired form. They are all almost invariably symmetrical, and they are all subject to the law of spontaneous decline. The persisting and aggressive forms of local disease, so common in the late stages of the acquired disease, are almost unknown in the subjects of inherited taint. Lupoid affections of the skin are the commonest form of tertiary acquired disease; they are almost never seen in that which is inherited. When keratitis of the interstitial form occurs in the subject of acquired disease (very rare) it is always amongst the secondary phenomena: in the inherited disease it may occur very late, but it is almost always symmetrical, and always transitory. The same is true of otitis, which occasionally leads to symmetrical deafness in subjects of acquired disease, but very often in those who inherit it. We have been so much in the habit of regarding persistent nodes as tertiary that it is difficult to think of them in any other sense; yet, undoubtedly, in the acquired disease a general tendency to slight periostitis, usually symmetrical, is often observed in the secondary stage; and now and then large swellings are produced. These pass away, and after, it may be, a long series of years, we encounter the tertiary nodes which are asymmetrical, and which persist unless cured by treatment. Now in hereditary syphilis, although the osseous system often suffers severely, we rarely see anything resembling the tertiary kind of node. The tendency to periostitis is also transitory, and it does not recur in adult life. It ceases, too, irrespective of treatment. The gummas of the tongue which are so common in acquired syphilis are scarcely ever seen in the inherited form. It may, indeed, be asserted that there is very little to contradict the view that in inherited taint the secondary phenomena may be spread over many years, and that of tertiary ones, parallel with those seen in the acquired disease, we have almost no evidence. The explanation of this latter fact is perhaps to be sought in the more rapid and complete metabolism of tissue during youth and adolescence, by which the system is more thoroughly purged of all morbid material.

Conclusions as to the transmission of inherited taint. The following appear to me to be well established :—

1st, A child may inherit syphilis in a severe form from but one parent—from its father alone, or from its mother alone.

2nd, When both parents are the subjects of syphilis a child is more certain to suffer, and is perhaps more likely to suffer severely, than when only one is infected.

3rd, We have as yet no data on which to ground an opinion whether a child is more likely to suffer severely when its father is the source of contamination than when it derives the disease from its mother; or the reverse.

4th, In a large proportion of the cases met with in practice, the taint is derived from the father only.

In connection with the hereditary transmission of syphilis, an exceedingly important question arises, *whether any degree of taint is transmissible to the third generation.* There is no doubt that persons of marriageable age often present heredito-syphilitic lesions in an active stage, such as keratitis and nodes. I have repeatedly seen patients of various ages, from twenty to eight-and-twenty, become the subjects of syphilitic keratitis for the first time. We might conjecture that such persons would be likely to transmit to their offspring some degree of taint, seeing that the taint is still in activity in their own bodies. I am not aware that any facts have as yet been published on this subject. Conjectures abound, and several surgeons have expressed their belief that the influence of syphilis once acquired is felt through several subsequent generations. About eight cases have come under my own observation in which persons, undoubtedly the subjects of inherited disease, have become parents. With one doubtful exception, I have never been able to discover any evidence of disease in the offspring. In several instances the offspring have appeared to be in excellent health. I have always made a point of seeing the children for myself, never relying upon the parents' statement— a precaution which is essential.

It is very important to realise that *during the secondary or febrile period of syphilis every tissue in the body is more or less affected* by the poison. Although we are accustomed to speak of sore throat, eruption, iritis, and so forth, as the secondary symptoms, yet in naming them we instance only those which are most conspicuous, and by no means all. Although in a majority of instances from first to last there may not be any indications whatever of general tissue-implication, yet we must accept it as a proven fact that such is the case. The accidents which have happened in syphilitic vaccination, as well as many other occurrences, prove that during this stage of the disease the most minute quantities of the patient's blood, or of the serum secreted by an abrasion, may prove fully contagious and produce the complete disease in another person. How soon this vital activity of the virus in the blood usually ceases, and how long it is possible for it to last, are very important questions to which as yet no definite answer can be given. That it does not last indefinitely, and that in a large majority of cases it ceases within a comparatively short period, say within a year or eighteen months, is made probable by a large body of circumstantial evidence. Syphilis in married life would be far more common than it is if this were not the fact. Thousands of men marry at or about the end of two years after primary syphilis, and many at much shorter periods; yet the instances of communication of the disease to their wives and children are but infrequent. On the other hand, if marriage take place within a year of the primary disease, it is perhaps exceptional for the children to escape, and by no means uncommon for the wife to acquire a chancre. What I have named for convenience the "*after-marriage chancre*," is a temporary sore occurring in connection with intercourse immediately after marriage on the penis of a man who has formerly had syphilis. Of these I have seen several remarkable examples with their results of chancre and secondary syphilis in the newly-married wife. It seems to be possible that such sores may be produced at a period as long as two years after the primary disease, and in cases in which the man has long appeared to be quite free from symptoms. Fortunately they are extremely infrequent. For my present purpose, however, they suffice as proof that the virus of syphilis may live on in the patient's blood during the long period mentioned; and this too, in some instances, in spite of much treatment by mercury. Their rarity, I repeat, may also be permitted to demonstrate the converse proposition that in a very large majority of cases the virus does not so survive.

What has just been asserted as regards the general diffusion and possible persistence of the virus in the blood must be admitted also as a possibility in reference to all the viscera and all the tissues of the body. Putting aside as unquestioned the affection of the skin and mucous membranes, it may be well to say a few words respecting the nervous system and its appendages, the arterial system, and the bones.

Nervous System.—Fournier has taught us that in some cases in the secondary stage of syphilis the patient experiences a general loss of sensibility to pain in the skin. This curious condition he met with chiefly in young women who were much reduced in health. This class of patients has not been much under my own observation, and I am not able from my own experience to say much in corroboration of the statements of this distinguished observer. That symptoms of nervous disturbance, sometimes local and sometimes general, do however occur in the secondary period of syphilis, there can be no doubt. I have seen and recorded a few instances in which a state of general paralysis involving both motion and sensation occurred, and the patient was apparently saved from impending death only by the very prompt use of mercury. In another very important group of cases the spinal cord appears to be the seat of myelitis in its lower part only; and a temporary condition of paraplegia, which may be almost absolute as regards both sensation and motion, and which involves the sphincters, may be established. In some of these cases the upper extremities are more or less involved also, but usually they escape. The paraplegia is generally symmetrical, though not quite always. A very remarkable corroboration of the diagnosis that this affection depends upon a temporary inflammation of the secondary type is obtained from the facts that it is usually curable by vigorous treatment, and that once cured it shows no tendency to relapse. In these features it corresponds with what we know of the otitis, iritis, and other affections of the secondary stage, which are probably its analogues. It may be noted also that it differs widely from the tertiary affections of the nervous system, which are usually aggressive, and which tend to relapse after apparent cure. Inflammations of the sense-capsules—the eye and the ear—although exceptional, are not very rare in the course of secondary syphilis. They are usually acute and transitory, but unless very promptly treated may result in much damage to the organ. Affections of single nerves, as denoted either by paresis or by very severe pain, may occur in almost any region during secondary syphilis, but they are rare.

That the *osseous system* is implicated during the secondary stage is often proved by the presence of what are called osteocopic pains or syphilitic rheumatism. These pains are not very infrequently accompanied by local periosteal swellings of the most definite character, but differing from our ordinary conception of a node in that they are very transitory, never tend to suppurate, and leave no perceptible thickening behind them. They are sufficient, however, to prove that the periosteum does inflame during the secondary stage.

If we turn to the *arterial system* we find facts of the utmost importance, although somewhat difficult of interpretation. It appears probable that in many if not in most cases of syphilis the whole arterial system suffers more or less during the earlier stages, and that certain changes take place in the arterial coats, more especially in the intima, from which the recovery may never be absolutely complete. The arteries may remain through life liable to take on other forms of disease, under the influence, it may be, of local exciting causes; hence aneurysms, thrombosis, endarteritis obliterans, and their results in hemiplegia and other forms of paralysis. It would appear probable that at various stages of syphilis it is possible for a single arterial trunk to become involved in changes which produce a considerable narrowing of its calibre and a corresponding diminution of the supply of blood to its territory. In interpreting some of the phenomena of nervous disturbance, it is often extremely difficult to say whether they are primary to the nerve structures themselves or only secondary in consequence of arterio-capillary disease. There yet remains much for the pathological anatomist to elucidate in this matter.[1]

Tertiary Symptoms or Sequels.—I have endeavoured to draw a fairly strong line of distinction between secondary and tertiary symptoms. The secondary phenomena constitute a stage; they come on at a certain known period; they are in their nature transitory, and undergo spontaneous cure; they affect the two halves of the body at the same time, proving that they depend upon blood-poisoning; when once passed they rarely return. The tertiary symptoms are not so properly a stage, but must count rather as the sequels, more or less accidental, of the preceding stages. They are as a rule not symmetrical, which makes it seem improbable that they depend upon blood-taint; they have no tendency to spontaneous cure—quite the reverse. They relapse over and over again after remedial treatment. The period which intervenes before their outbreak is of very different length in different cases, and in many they never occur at all. From these facts we infer that they are due rather to the altered constitution of the affected structures than to any free virus still circulating in the blood.

We may briefly enumerate the principal tertiary symptoms as they occur in relation to special organs or structures. *First, the skin and mucous membranes.* Tertiary affections of these tissues differ in a most marked manner from those which occur in the secondary stage. With the exception, perhaps, of palmar psoriasis, they usually involve ulceration of greater or less depth, and consequently leave cicatrices. Very frequently the patch assumes a crescentic form, spreading at its edges and healing in its centre,—the well-known "horse-shoe" or serpiginous ulcer. If the disease begin in the middle line it may spread equally on the two sides, and may thus appear to be symmetrical; but it is decidedly unusual for symmetrically-placed patches to appear on the opposite limbs, or on corresponding parts of the trunk. In many cases the skin is involved secondarily to the subcutaneous cellular tissue, the disease having begun as a gummous tumour or node of the cellular tissue. A form of lupus attended by rapidly-spreading phagedænic ulceration occasionally occurs in tertiary syphilis; but there is good reason for believing that the common forms of lupus, whether exedens or non-exedens, have no connection whatever with syphilitic taint. The appendages of the skin, the nails and hair are frequently affected during the secondary stage, and but very rarely at later periods.

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[1] We are indebted to Dr. Bristowe for some of the earliest and most trustworthy investigations in reference to the disease of the arteries in syphilis. In Germany Dr. A. Wagner was one of the pioneers. Dr. George Oliver, in the course of his researches in arterial pressure and variations in the calibre of arteries in different positions, came upon the very remarkable observation, that in the subjects of syphilis (in all stages) the radial artery continues uniform in size in the erect and recumbent postures. This he found so constantly the case that it was impossible to attribute it to local or exceptional disease. He believes that it indicates some change in the arterial coats of such a nature as to elude recognition by the finger, which cripples the physiological play of the tube.

The most frequent affection of the mucous membranes which we encounter in connection with tertiary syphilis is a rapidly-spreading ulceration of the palate and pharynx. This again is totally different from the throat affections which occur in the earlier stages. Instead of being superficial and marked chiefly by swelling and inflammatory deposit, it is characterised by deep ulceration and loss of tissue. Instead of showing itself symmetrically on the two sides, it commences at one, two, or more points, and spreads quite irregularly. The scars left by these deep ulcerations not infrequently narrow the pharynx and occasion difficulty in deglutition. In a few cases the ulceration may extend down the œsophagus, and in many the larynx is involved. Every now and then we see cases of tertiary syphilitic ulceration of the mucous membrane of the rectum, and again we must note that it is ulceration, and that it is not attended by the development of the condylomas or mucous patches of secondary syphilis. Stricture of the rectum is much to be feared when these ulcerations heal. Several authors have described cases resembling dysentery in all their symptoms, but occurring in syphilitic patients, and cured by anti-syphilitic remedies. Sir James Paget has recorded a case of this kind, and I have myself seen some very well-marked ones. It is probable that in such cases ulceration of the mucous membrane is present at a considerable distance above the anus. I have seen several cases in which syphilitic ulceration extended higher than the finger could reach.

The cellular tissue is frequently involved in common with muscle, with periosteum, or with fascia. In not a few cases, however, we meet with what are called cellular nodes, in which the disease begins; and, up to a certain period, it is confined to this tissue. These may occur in any part of the body, but are much more usually met with in the lower extremities than in any other part. They are very common close to the knee, and especially so in women. It is a very interesting fact that these cellular nodes are comparatively very infrequent in men. Whether this is to be explained by the greater abundance of cellular tissue in women, or by the fact that many women obtain syphilis in a manner wholly peculiar to them—that is, by fœtal contagion—may be open to some question: probably both influences have their share in the result.

In the early stage of a cellular node we find a small lump of induration often exceedingly tender. At first it is firm, but as it extends it becomes doughy and softer. When of considerable size there is frequently a very deceptive sense of fluctuation in it. The overlying skin becomes adherent and of a dusky red colour. At length ulceration takes place, and a large core is exposed, consisting of sodden and infiltrated tissues, much resembling soaked wash-leather in appearance. Unless specific remedies be used, this core is very slow in separating, and the ulceration of the skin over it may spread widely.

Cellular nodes are not infrequently multiple, but more usually single. The patient frequently has scars of former ones on the opposite limb, but it is exceptional to find them simultaneously present on corresponding parts.

A period varying from four to ten or fifteen years has usually elapsed between the occurrence of primary contagion and the development of cellular nodes. In close connection with syphilitic inflammation of the cellular tissue we must mention that of *subcutaneous bursæ.* It is not at all uncommon for a bursa to suffer in connection with the disease of the tissue around it, and sometimes there appears to be clear evidence that the disease began in the bursa itself. The bursa in front of the patella is the one most frequently involved.

The joints themselves may be occasionally implicated in tertiary syphilis. Usually they are involved secondarily in connection with periostitis of the bones which form them. In the secondary period rheumatoid pains in joints are common, and in inherited syphilis symmetrical effusion into the knee-joints often coincides with the keratitis: it is always transitory. Chronic affections of joints in the tertiary stage of syphilis, and in connection solely with it, are exceedingly rare.[1]

Inflammations of the periosteum and bones have long occupied the most prominent place amongst the tertiary symptoms of syphilis, and they are still some of the most common. In enumerating the symptoms which characterise the secondary stage we have mentioned pains in the bones, attended occasionally by slight and temporary swelling. This kind of periostitis, however, never lasts long, and, so far as my own observation goes, never leads to suppuration. Tertiary nodes seldom occur until at least two years have passed since the first contagion, and generally the period is much longer. They may affect almost any part of the osseous system; but the bones which are superficial, and therefore most exposed to external influences, are those most frequently attacked: for example, the calvaria, the tibias, and the clavicles.

The bones of the palate, the alveolar processes of the maxillas, the vomer, and other bones in the nasal passages, are very frequently affected; and when such is the case exfoliation of portions usually occurs.

Syphilitic periostitis may vary considerably in its degree of severity and in its tendencies. In some cases there is but little acute inflammation, and the result is a great thickening of the bone affected, without the occurrence of suppuration. This frequently occurs in the bones of the skull—the whole calvaria acquiring greatly increased thickness and density. It is also not uncommon on the surface of the tibia and other long bones, constituting what is known as the osseous node. In other cases suppuration occurs, and in these very frequently large portions of cellular tissue become involved, and we have a swelling consisting in part of a periosteal abscess and in part of a cellular node. When the bone is exposed by ulceration exfoliation of portions often results.

When the bones of the skull are attacked by syphilitic periostitis it is very possible that inflammation may occur internally as well as superficially, and that we may have symptoms referable either to irritation of the cerebral coverings or to compression consequent upon intra-cranial abscess. In association with nodes on the skull various symptoms of mental disturbance show themselves: extreme irritability of temper, liability to fits of uncontrollable passion, melancholia, and even acute mania may occur. These symptoms of *mental disturbance* may or may not be associated with those of local paralysis. They not infrequently result in attempts at suicide. The proof that they really are dependent on syphilitic lesions is afforded by the ease and rapidity with which they are relieved by the iodide of potassium.

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[1] Diseases of the joints in syphilis were the subject of a Course of Lectures by my son at the Royal College of Surgeons, 1890.

Periosteal nodes are not very frequently met with on the short bones; we must, however, be prepared to recognise them occasionally on these also. The patella and the os calcis are occasionally affected, and now and then the other bones of the tarsus or carpus may suffer.

Diseases of the muscular system occur chiefly amongst the most remote sequels of syphilis, and they are by no means frequent. They usually take the form of nodes, or gummas, developed in the substance of some single muscle. The induration is usually very considerable, and in many parts abruptly limited. The diagnosis from cancer is often very difficult, and many mistakes leading to unnecessary operations and to supposed permanent cure of cancer have occurred. The muscular substance of the tongue is the structure most frequently attacked by this form of gummatous growth, but it has been met with in almost all the muscles of the body. The sterno-mastoid, the masseter, the supra- and infra-spinatus, the gastrocnemius and the rectus femoris, may be especially mentioned. Some years ago I had under care an extremely interesting case in which a tumour, which we at first suspected to be cancer, was developed in the left masseter of a lady who twenty years before had suffered from syphilis. At the time the tumour appeared she presented no other syphilitic symptoms, and the correct history was obtained with much difficulty. The tumour wholly disappeared under the use of the iodide of potassium.

Some forms of syphilitic indurations of the tongue are in all their stages exceedingly difficult to distinguish from cancer. They are very hard, have well-defined edges, are painful, and when they ulcerate present an unhealthy surface. Iodide of potassium in full doses will usually clear up the diagnosis in the course of a week or ten days. The heart itself is sometimes the seat of syphilitic nodes. Of this, M. Ricord[1] was, I believe, the first to publish an example; but many others have been recorded by subsequent observers.

The Glandular System.—Chronic enlargements of the lymphatic glands, sometimes resulting in suppuration, are every now and then met with as the sequels of syphilis. It is a remarkable fact in reference to tertiary syphilitic lesions generally, that they do not cause any secondary enlargement of the adjacent lymphatic glands. This is true of syphilitic ulcerations of the skin and mucous membranes, of all the various forms of node, and of syphilitic tumours in muscles; and it often constitutes a very useful means of differential diagnosis between cancer and syphilis.

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[1] See *Traité complète des Maladies Vénériennes*, Planche xxix. In this instance the patient was a man aged 41, who had suffered from a chancre followed by constitutional symptoms eleven years prior to his death.

The Internal Viscera.—The investigations of modern pathologists have fully confirmed the conjectures of the older writers on syphilis as to the frequency with which the viscera of the trunk, and more especially the liver, suffer in constitutional syphilis. In connection with this subject we must especially mention the very valuable contributions of Dr. Wilks. As to the exact period in the course of the disease at which the viscera are attacked, it is difficult to obtain any positive evidence. What we discover in the post-mortem examination is usually the result of long past disease, and it is comparatively infrequent to find it in a recent stage. What evidence we have, however, favours the belief that it is not usually until the later periods that the viscera suffer severely.

The liver appears to be far more frequently affected than any other organ. Indeed, in the examination of the bodies of those who have suffered severely from tertiary syphilis, it is decidedly exceptional not to find some proof of hepatic mischief. The most common condition consists in large white patches of fibroid thickening on the surface of the organ. These patches are evidently cicatricial. The liver is knotted and puckered up by them, and cicatricial bands dip from the surface into the substance of the organ. Sometimes, when the destruction has been great, the whole bulk of the organ is diminished. In recent disease the affected parts of the organ are enlarged, and on section exude a material not unlike bees-wax, or glutinous and gummy. I am not aware that abscesses have as yet been met with in the liver in supposed connection with syphilis. Virchow recognises two forms of disease—a capsular hepatitis and an interstitial hepatitis. Of these the capsular inflammation is the more common and the less serious. It is probable that the two are generally associated to a greater or less extent. Ascites occurs every now and then in connection with syphilitic disease of the liver.

Testes.—Syphilitic sarcocele has usually been classed by authors as a secondary symptom. I feel sure, however, that this is not quite correct. It is amongst the earlier of the sequels, but it very seldom occurs during the secondary stage. It is commonly met with in conjunction with nodes, and with deep ulceration of the skin rather than with the superficial rashes of the secondary epoch. It consists in the free effusion of lymph (fibro-plastic material) into the substance of the testis, or, more rarely, into the epididymis.

The swelling often attains a very considerable size, and when it does so it presents the peculiar feature of feeling very light in the hand. Syphilitic sarcocele is much more frequently symmetrical than any other form of tertiary syphilis. This circumstance we might expect from the fact that it occurs much nearer to the secondary stage than do most of the others.[1] Still, however, it is only exceptionally symmetrical.

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[1] On this point Mr. Curling wrote: "Sir A. Cooper thinks that in the majority of cases the disease attacks both testicles. The eight examples recorded in his work do not, however, bear out this remark, for in only two of them does it appear that both organs were attacked. According to my observation the disease is more commonly confined to a single gland, though it occasionally affects both; and this also appears to be the opinion of Ricord."

Nervous System.—We come, lastly, to syphilitic affections of the nervous system itself.

I have previously adverted to the occasional occurrence of cerebral symptoms in connection with syphilitic inflammation of the bones of the skull, and to the formation of intra-cranial nodes; but, quite apart from disease of its osseous case, the brain itself may suffer directly from the formation of tertiary syphilitic deposits in its membranes, and yet more frequently from disease of its blood-vessels. We may also have deposits of like nature in the substance of nerve-trunks, producing special forms of local paralysis. To these isolated deposits the name syphilitic neuroma has been given, and many well-authenticated cases are on record in which the diagnosis has been confirmed by an autopsy. In a far greater number of cases the diagnosis has received an almost equally valuable confirmation in the cure of the disease by iodide of potassium. So frequently, indeed, is tertiary syphilis the cause of paralysis, that investigations in this direction ought never to be omitted in cases in which the nature of the disease is in the least doubtful. It is, indeed, safe to go farther than this, and to say that in all cases of paralysis without evident cause, and in which syphilitic antecedents are even possible, it is advisable to try the effect of iodide of potassium. I allude chiefly to cases of paralysis of the cranial nerves, for it would appear that neuroma is more frequent in them than in the spinal nerves.

Syphilitic affections of the nervous system may occur in any stage; they are often among the late tertiary phenomena.

Colles' Law.—About the year 1837 Mr. Abraham Colles of Dublin published the important observation that mothers who suckled their own syphilitic infants do not contract chancres on their nipples. If, on the other hand, a healthy wet-nurse be employed to rear a tainted child, a nipple chancre, to be followed by constitutional syphilis, is not an infrequent result. Subsequent observers have unanimously confirmed Mr. Colles' statements of the facts, although, as might have been anticipated, a few exceptions have been recorded. Preferring to give weight to these exceptions rather than to the great mass of confirmatory evidence, some have even suggested that what has been called Colles' law is at the most of but doubtful force. They contend that chancres of the nipple in wet-nurses are very rare, and those which occur in mothers not very infrequent; so that in reality no great difference between the two classes can be proved. This argument will, however, be seen at once to have no validity when we remember that it is extremely rare for a wet-nurse to encounter risk, whilst for mothers to do so is an everyday occurrence. If mothers were in as much risk as wet-nurses we should see chancres of the nipple very frequently indeed. A surgeon who was responsible for a wet-nurse giving her breast to a syphilitic child would, if syphilis ensued, become liable to an action for damages. No well-informed medical man ever does permit such a thing, and the number of cases in which healthy women spontaneously give their breasts to infants with syphilitic mouths must be very small indeed. We may then assume that what has been called Colles' law does express a well-established and very important clinical fact.

It follows from Colles' law that a woman pregnant with a syphilitic child does receive from the fœtus something which renders her immune to the contagion of the disease. It is, however, most certain that in the course of her acquisition of this immunity she but rarely exhibits any well-marked secondary symptoms. It is common for a married woman to bear a tainted child, she having been, through her whole pregnancy and before it, quite free from obvious symptoms. We have proof, then, that the blood transference which occurs between fœtus and mother may produce immunity without causing an outbreak, and this is a very important observation. To what extent such mothers are liable in the future to phenomena of the tertiary class is a question which it is very difficult to answer. That they do so suffer, not infrequently, seems to be well established; and is a corroboration of the belief that they do really receive infection during pregnancy.

When a man who has suffered from syphilis, but who believes himself cured, enters into marital relations with a healthy woman, the latter encounters risk of two different kinds. It may happen that a new excoriation on the penis may be produced and that it may cause a chancre in the woman. In such case all the usual phenomena of syphilis will probably in due course ensue. If this risk be escaped, it is not probable that the woman will suffer in any way unless she become pregnant. There is no reason to suppose that syphilis can enter the system without a primary sore, or that the semen, or other secretions of the husband, can convey it. The second kind of risk will be encountered if the wife become pregnant. Whether it be possible for a paternally tainted fœtus to produce in its mother a severe outbreak of secondary syphilis must be held to be doubtful. Many cases are on record supposed to be examples of such occurrence, the wife having shown abundant evidences of blood infection during the early months of pregnancy. In all such, however, there is the fallacy that a primary sore may possibly have been overlooked. On the other side cases are innumerable in which a young wife remains in perfect health, never manifesting the slightest indication of disease, and yet bears an infant destined to show it. The latter is certainly the rule, and the former, if it ever occurs, is the exception.

Abrasions on the penis in newly-married men who have had syphilis are not uncommon, and not infrequently prove infective to their wives. These seldom last long or attract much attention, and unless inquired after may be easily overlooked and forgotten. I have given to these abrasions the name of "the after-marriage sore," and have published three examples of their occurrence at periods as prolonged as two years after the original disease. The abrasion usually occurs in the site of the first chancre. Fortunately such sores are exceedingly rare in those who observe the precaution of allowing an interval of not less than two years to elapse.

A few words may be suitably inserted here as to the possibility of a mother who acquires syphilis during her pregnancy communicating the disease to her fœtus. The facts which have been recorded are to my own mind quite conclusive on this point. At whatever period of pregnancy the disease is so acquired up to the last four weeks, it is almost certain that the fœtus will be infected. So far as facts yet recorded permit an opinion, no difference will be observed in the phenomena displayed by the child from those of the ordinary form of inherited syphilis.

Marriage in reference to Syphilis.—Before proceeding to discuss this question I may at once aver my conviction that a great amount of human happiness is frustrated by the exaggerated fears which are entertained by the profession and the public. Not only are marriages needlessly deferred or altogether prevented, which had they been permitted would have produced only mutual good and blessing, but, on the other hand, unhappy and immoral connections are distinctly multiplied. When a young man is forbidden to marry because he has had syphilis, or when his own fears or what he calls his "sense of honour" prevent him, it does not by any means follow that he will lead a continent life. We have but to look at the subject in the aggregate to see how important are its bearings. It may seem but a little thing in an individual case; but what we have to remember is that syphilis in young men is and always will be very common, and that the cases are really very numerous. If we suppose a thousand young men otherwise wishful to marry, and in circumstances to do so with prudence, deterred from it by the fear of syphilis, we must realise that an equal number of young women must also at the same time lose their chance of marriage. Now, supposing that a period of two years has been passed since the primary disease in the man, the amount of risk which is run is probably infinitesimally small. That there is still some little risk no one acquainted with the facts would be prepared to deny. Shall we on account of that little danger at once lengthen the period to three, four, or five years? I believe that to do so would be to act unwisely. In this matter the profession should take the part of the reassurer and not of the alarmist. The fears of the public are far in excess of what the facts warrant. Many marriageable men, for whom marriage would have been perfectly safe, yet remain bachelors for years, or perhaps for their lives, from the consciousness of having had syphilis. If a similar degree of scrupulosity were to be observed in reference to the risk of transmitting tuberculosis or scrofula, or the neurotic diathesis, or that of arthritis or of cancer, we should have but few marriages. Yet the physical evils and suffering produced by these inheritances far exceed those which result from syphilis. Compared with them, inherited syphilis is both rare and easily curable, and were it not that a certain stigma attaches to it as a "foul disease," and one for which the parent is morally responsible, it would receive but little attention.

In past years those who had suffered from syphilis were allowed to marry as soon as all symptoms had disappeared, and often within a very few months of the primary disease. Inasmuch as there is no reason to believe that infantile syphilis was much more common then than now, we may believe that in many instances a period of six months is quite adequate to free a man from the risk of begetting a syphilitic child. We know that in a large proportion of cases the patient himself becomes permanently free from manifestations within that period; and this fact may help us to the belief that the virus does really perish from the blood so as to make transmission impossible. It must be admitted, however, that in very many others it lingers much longer. The rule which now prevails widely of forbidding marriage for two full years from the date of the primary sore is probably a safe one. It may possibly be relaxed occasionally under exceptional conditions when the symptoms have disappeared very early and very completely; and there may be others in which the converse has been the case, in which a yet longer period should be required. It would, however, be a pity to make the general rule insist on more. It is foolish to concentrate our attention on a few exceptional cases and to forget the lessons taught by the vast majority. If the patient during almost the whole period have been efficiently treated with mercury, the absence of risk may be asserted with the greater confidence; but we must always remember that time as well as mercury cures syphilis.

The rule for the woman in this matter is probably the same as that for the man; but it is perhaps true that the risk of transmitting syphilis to offspring lasts longer in women than in men,—that is in the germ than in the sperm.

Treatment.—Respecting the treatment of syphilis a few general principles may easily be advanced.

In the first place, it is quite certain that all its early phenomena have a definite tendency to spontaneous disappearance. It is upon this well-established fact that the non-mercurialists build their hopes. The chancre, however large and however hard, will in time melt away; the hardened glands and the skin eruption will also disappear. In a majority of cases these primary and secondary phenomena will not assume any great severity, and the patient will never be seriously ill. It is, perhaps, in not more than half or even in a minority of cases that the disease assumes serious features. In those in which it does so, the degree of severity will vary within very wide limits, and in a certain proportion the severity of the fever, eruption, and other symptoms, may be such as to endanger life. In some also we know that the secondary stage will never disappear, but will pass on into conditions characteristic of the later one.

A second general proposition is, that over all the early manifestations the mineral mercury, in whatever form it may be introduced into the system, exercises a specific influence. It causes the induration of a chancre to disappear and the sore to heal, it makes the eruption vanish, it brings down the febrile temperature if such have been present. The details of its influence will vary with the modes of its administration and the idiosyncrasies of the patient, but about these main facts there can be neither doubt nor dispute.

Our third proposition is that over the tertiary manifestations of syphilis—the gumma—whether of skin, cellular tissue, coats of artery, cerebral meninges, or periosteum, the iodide of potassium exercises almost as definite an influence as does mercury over the earlier ones. Under its influence large gummas will disappear, periosteal pains will cease, and ulcers will heal.

Whether any other drugs, mineral or vegetable, exercise any specific influence over syphilitic processes is as yet not proven. It may be held as scarcely likely that mercury and the iodides are the only remedies which possess such powers; but although much has been from time to time asserted, nothing beyond what has been just stated has received the imprimatur of professional experience.

In the discussion of details it may be convenient to take the last of our statements first. All are agreed that in the tertiary stages the iodide of potassium must be used. Since its introduction, indeed, the terrors of this stage have to a very large extent vanished. The iodide should be given in doses suited to the idiosyncrasy of the patient and the resistance of the malady. There is no remedy in which idiosyncrasy counts for so much and in which dose may vary within such wide limits. It is well to begin with small doses, invariably to combine ammonia with it, and to increase the dose only if required. Sometimes minute doses, of a grain or even a third of a grain, will exercise as definite a curative influence as thirty times the quantity may do in another patient. It is, as a rule, not well to give it long continuously, but to omit it for a few days at a time, and to begin anew with a smaller dose. In cases of idiosyncrasy, in which it exercises an injurious influence, and brings out eruptions or causes œdema of mucous membranes, all that is needed is to reduce the dose sufficiently. In many cases the three iodides, of potassium, sodium, and ammonium, may suitably be combined. Whether these salts be given together or not, in no case must the addition of ammonia be forgotten; it is reputed, and with reason, to double the effect of the dose. Iodide of potassium has for many persons heavy drawbacks. At the same time that it cures the syphilitic lesion it often depresses the general tone, lowers the spirits, and entirely incapacitates the patient for the enjoyment of life. Indiscriminately used, as it is by many at the present time, it is productive of much wretchedness, which might, by a little care, be avoided.

The use of mercury in syphilis has been the subject of almost endless debate and difference of opinion. It may be given in very various methods and in very different doses. In order to avoid prolixity, I will begin by describing in a little detail the plan which I think by far the best; namely, that of the continuous use of small doses over long periods. By it, if begun early enough—that is, before the appearance of secondary symptoms—the evolution of the disease may be wholly averted, and not a single symptom beyond those of the primary stage may be allowed to appear. It is difficult to conceive any better result than this. The preparation which is the most easily managed is the gray powder (hydrargyrum cum creta), and there are obvious advantages in keeping as much as possible to one form. The dose should be one grain only, given in pill in combination with opium, and repeated as frequently as the patient can bear it. It is most important to begin with sufficient opium, so as to be secure against diarrhœa at the onset. A fifth or even a fourth of a grain in each pill is not too much. Should it cause headache, drowsiness, or constipation it can easily be reduced. The two complications to be avoided are salivation and diarrhœa. The problem is to introduce as much mercury as possible without the occurrence of either of these. The diarrhœa is to be prevented by opium and attention to diet, the salivation by frequent cleaning of the teeth and the use of an alum mouth-wash. The pill suggested should be given four, five, six, or seven times a day without regard to meal times. On no account should the patient be allowed to take two together; by dividing the doses inconveniences are avoided, and the desired effect produced with much greater certainty. All soups, green vegetables, fruit, and malt liquor should be strictly forbidden. The patient should be advised not to smoke, and should be told that he will have to carry out the treatment for six, nine, or twelve months without any intermission. In very few cases will it be found desirable to make the dose of mercury larger.

An experience of many hundred cases treated according to the above plan justifies the statement that if it be faithfully carried out syphilis may be wholly suppressed, and the patient may never know anything about his malady beyond its primary symptoms. In many cases he may come to doubt the diagnosis on account of the completeness of his cure.

Some very curious facts have been observed in connection with this continuous treatment with the object of suppression. If at the end of four or five months, during which the suppression has been complete, the mercury be left off, there will usually appear at the end of a month or six weeks a very definite secondary and symmetrical eruption. It will, however, be a very slight and mild one, and will disappear very quickly when the remedy is resumed. Of the secondary symptoms, sores on the tonsils are those most difficult to prevent; and many patients who wholly escape eruptions yet show a slight form of the characteristic sore throat. This may be because the throat usually suffers very early; or it may be that mercury is occasionally the cause of congestion of the pharynx. During the course of treatment suggested the patient need take no special precautions. He may live as usual and follow his avocations. He should not, however, use tonics, either as drugs or in the form of sea-bathing, nor out-of-door exercises. The more closely he keeps his house and the longer the time that he spends in bed the less will be the quantity of mercury required. Ptyalism, if it occur, must be regarded as an accident, and not in the least as proof that enough mercury has been given. It must be remedied as promptly as possible, kept at bay by constant cleansing of the mouth and teeth, and the mercury continued.

During the treatment the patient will lose fat but not flesh. He will retain his strength, but may fail a little in weight. At the end of it he will probably declare himself in better health than ever before in his life.

Under certain circumstances, but not often, it may be well to combine iodide of potassium with mercurial treatment in the secondary stage of syphilis. This will be the case if the bone pains are severe or if the mucous membranes suffer severely. Provided, however, that the mercury have been begun early enough, such symptoms will seldom occur.

It has seemed best to state the ordinary result of the suppressive treatment by mercury before considering whether mercury ought or ought not to be used. If the statements just made are well founded there can hardly be a doubt about it, since the advocates of abstinence from specifics cannot but admit that, although many patients do well, many others suffer very severely. The same remark applies also to other methods of using mercury, for of none can it be alleged that less trouble, or less expense, or less risk of loss of health to the patient is involved. Better results could not possibly be obtained. Whilst, therefore, it is to be admitted that the inunction method, that by subcutaneous injections, and that by the vapour bath, are all of them exceedingly useful, it is yet difficult to find advantages in any of them over that recommended. The estimation of the results of treatment in syphilis has two aspects: first, the prevention of inconvenience and loss of health during the secondary stage; and, secondly, the prevention of sequels and of tertiary symptoms. That in regard to the former mercurial treatment is triumphant there can be no reasonable doubt. It is, however, a very different thing and much more difficult of accomplishment to prove that it is influential in avoiding the latter. To do this it is needful to collect indifferently the case-histories of many patients extending over the whole life subsequent to the attack. Whilst, however, it may be admitted that no plan of treatment, however successful at the time, can be held to secure the patient against subsequent risk, there is much to be said in favour of the belief that it is a decided gain to suppress, or, if too late for suppression, quickly to cure the secondary stage. Many facts favour the belief that gummas usually appear in the sites of former syphilitic lesions, and if so, it must be a gain to prevent the development of the latter altogether. Further, nothing is more certain than that those who suffer severely in the secondary period often do so also in the later ones. All the cases of so-called "malignant syphilis" are instances of a severe secondary stage imperfectly combated. Under the suppression plan none such ever occurs.

Diagnosis of Acquired Syphilis. — The recognition of syphilitic symptoms in the *secondary stage* is not usually difficult. The copiousness of the rash, its symmetry, the copper-tint, the frequent coincidence of different types of skin eruption in the same case, the presence of febrile disturbance, the absence of cutaneous irritation and the coexistence of sores in the tonsils — and frequently on the mucous membrane of the cheeks also—are all features which help to make the diagnosis easy and certain. To these we may add that the syphilitic exanthem usually appears first on the abdomen, chest, and fronts of the arms, that it very commonly affects the face, and that it avoids the backs of the elbows and the fronts of the knees, localities which are almost always attacked in cases of common psoriasis. Although syphilitic rashes vary very much in outward characters, yet in the features just mentioned they have always a basis of close similarity.

When mistakes occur they are usually those of insufficient attention. The patient is allowed to show only a small part of his surface, instead of being made to strip, or at any rate to expose the whole of his bust. If the latter course be adopted, the symmetry of the rash and its other peculiar features will almost always arrest the attention of the observer. Amongst minor points which occasionally assist may be mentioned the gyrate or ringed form of the patches; and in some cases of syphilitic psoriasis the comparative absence of desquamation.

The cases which cause most difficulty are those in which syphilis occurs in a patient who is already the subject of some other skin disease. In hospital practice it is very common to see scabies and a syphilitic rash coexisting, and in some such it is most difficult to pronounce with certainty as to the nature of the eruption. Examination of the mouth and throat and of the genitals will often remove doubt; but, if not, a few sulphur baths will usually prove a successful means of diagnosis.

Next to that of the exanthem itself comes the diagnosis of the *relapses of eruption*, which often occur between the secondary and the tertiary epochs. In these there is rarely any copious outbreak, usually only a few isolated patches. These are most commonly met with in the palms of the hands or soles of the feet, or on the front aspects of the forearms or legs. They are almost dry and attended with peeling of the epidermis. Very frequently there are small sores in the mouth or on the tongue; at the same time a form of acne, chiefly affecting the forehead, and leaving little pits or scars, is very often seen in this stage. If iritic adhesions be present, or if there be pits in the skin of the face and trunk, left by a former rash, the suspicion is much strengthened.

Lastly, we must consider the recognition of the various diseases which come into the category of *tertiary symptoms*. When these occur, it is often many years since the patient has suffered from any other, and it is quite possible that he may appear to be in excellent health. A few of the tertiary symptoms have been so long recognised in relation to their true cause, and are so rarely met with in connection with any other, that in themselves they almost constitute their own diagnosis, and often also help us to that of more obscure lesions. Periosteal swellings or nodes are the chief of these. To speak generally respecting other forms, we may say that the diagnosis must be founded in part upon the patient's previous history, in part upon any still existing remnants of former disease—such, for instance, as iritic adhesions—and in part upon the peculiarities of the disease itself. As regards the patient's antecedents, I may just remark, by way of caution, that we must not hastily assume that he is syphilitic because he tells us that he has had the venereal disease. A soft chancre with its suppurating bubo, or even an attack of gonorrhœa, although both of them quite innocent as regards constitutional infection, often leave more vivid impressions on the patient's mind than do an indurated sore and its exanthem. Those who are most ready to suspect in themselves a venereal cause, are often those who have never had true syphilis at all. If, however, there is a clear history of a chancre, followed by secondary rash, sore throat, and so forth, then we have obtained a fact which, whatever may be the present ailment, may be safely permitted to modify our treatment. The majority of tertiary lesions are by conventional usage regarded rather as surgical than medical, and it would be out of place here to speak in detail of the diagnosis of ulcers, gummous tumours, and so on. I may briefly remark that the serpiginous form of ulceration, healing in the centre and spreading at the margin, is a feature always to be regarded with suspicion; and I may repeat that tumours in muscle, which will wholly melt away under the influence of the iodide, are sometimes as hard and as defined as any variety of cancer, and have often led to needless operations.

In cases of disease of the nervous system in which syphilis is suspected, an examination of the patient's eyes, throat, tongue, and tibias should never be omitted. The existence of iritic adhesions, of scars of the soft palate, or of periosteal nodes, will often decide the question. The occurrence of nocturnal exacerbations of pain also is always suspicious. If the disease implicate only one nerve-trunk, especially if only one cranial nerve be involved, the suspicion of syphilis becomes very strong. Probably a full half of the cases of paralysis of the third, fourth, fifth, and sixth nerves, when such paralysis affects only one nerve, are due to syphilis, and are curable by specific treatment. In these cases the disease is hardly ever symmetrical, and the paralysis is usually complete. The seventh nerve is occasionally attacked, but not so frequently as the others. The nerves of special sense are not so frequently affected in acquired syphilis as they are in the inherited form. Nevertheless, cases do occasionally occur in which amaurosis or complete deafness is met with in the subjects of syphilitic taint, and without other assignable cause. In these the loss of function is usually symmetrical, and probably depends upon disease of the cerebral centre rather than on neuroma of the nerve-trunks. I am not aware of any cases in which paralysis of the branches of the eighth pair have been traced to syphilis, but no doubt such occur and might be recognised by due search. Paralysis of single nerve-trunks of any of the spinal plexuses—more especially of those of the brachial plexus—are now and then encountered.

The diagnosis of inherited syphilis rests on somewhat different data. Indeed, the whole course of the disease, as thus transmitted, presents some remarkable features of difference which I have endeavoured to bring into clear contrast in the appended tabular parallel. (See p. 283.) Some local lesions, not infrequent in those who have inherited the taint, never occur at all in those who have acquired it, as for instance interstitial keratitis. Others present important modifications of character; thus, when periosteal nodes occur in children, they are much more extensive than they usually are in adults. Speaking generally, the so-called "tertiary" symptoms of inherited syphilis, however long the interval of latency may have been, are for the most part symmetrical. We have seen that those of acquired syphilis are but rarely so.

The early stages observed in the course of inherited disease are very similar to those of the acquired form.

In the infantile period we recognise syphilis by the peculiarity of certain single symptoms; or, more frequently, and with greater certainty, by the peculiar grouping of several different symptoms. First in importance is the rash on the skin. The rashes, as in acquired syphilis, may vary much in their character, but the commonest are the erythematous or papular. If it be erythema the redness will show itself in abruptly margined patches, and will be characterised further by its peculiar red or coppery tint, compared by some authors to that of the lean of ham. Sometimes we see instances of dry, scaly rashes in infants, but these are rare. Pustular, vesicular and bullous rashes are also not infrequently witnessed. Condylomas at the anal orifice are common, though less frequent during the first few months than at later periods. At the same time as the rash, the little patient almost always displays the characteristic symptom known as "snuffles," and there is usually inflammation of the mucous membrane of the mouth and sores at its angles. Iritis occurs in a few cases, has similar tendencies to those seen in the acquired form, and is equally under the influence of specific treatment. It occurs also at the same stage, always amongst the secondary symptoms. Inflammation of the deep-seated structures of the eye—of the vitreous, retina, choroid—are as frequent as they are in the adult, and present the same characters. In some cases there is a slight form of diffuse periostitis of the skull-bones, and more rarely inflammation may occur at the junction of the epiphysis and shaft in many long bones.

During the stage of outbreak of the exanthem, which lasts, on the average, from the fourth week to the sixth month, the child becomes fretful, pale, and emaciated; growth is for a time arrested, and his shrivelled face resembles that of an old man. Emaciation is certainly the rule, but it has many marked exceptions, and we often see syphilitic infants who are fat and plump and look remarkably well.

At or about the age of one year, if the child have survived, it is usual for the secondary symptoms wholly to disappear. A period of latency now ensues, during which the child often enjoys very good health. Sometimes relapses occur, and such subjects are especially liable to be affected by condyloma. These relapses scarcely ever involve a return of cutaneous rash. I think that all observers will bear me out in the statement that the characteristic rashes so often seen in syphilitic infants are never witnessed at later periods of life. The tertiary epoch may begin at any period after the fifth year, but it is commonly delayed till at or near the period of puberty.

At or after the age of puberty the recognition of the subject of inherited syphilis may sometimes be made with great certainty; at other times it is surrounded by difficulties. Our most valuable aids are the evidences of past disease, more especially of the inflammations which may have occurred in infancy. A sunken bridge of the nose caused by the long-continued swelling of the nasal mucous membrane when the bones were soft, a skin marked by little pits and linear scars especially near the angles of the mouth, the relics of an ulcerating eruption, and protuberant frontal eminences consequent upon infantile periostitis, are amongst the points which go to make up what we recognise as an heredito-syphilitic physiognomy. Added to them we have very valuable aid furnished by the shape of the incisor teeth. In these patients it is very common to find all the incisor teeth dwarfed and malformed. Sometimes the canines are affected also. These teeth are often narrow, rounded, and peg-like; their edges are jagged and notched. Owing to their smallness their sides do not touch, and interspaces are left. It is, however, the upper central incisors which are the most trustworthy for purposes of diagnosis. When the other teeth are affected these very rarely escape; very often they are malformed when all the others are of fairly good shape. The characteristic malformation of the upper central incisors consists in a dwarfing of the tooth, which is usually both narrow and short, and in the atrophy of its middle lobe. This atrophy leaves a single broad notch (vertical) in the edge of the tooth; and sometimes from this notch a shallow furrow passes upwards on both anterior and posterior surfaces nearly to the gum. This notching is usually symmetrical. It may vary much in degree in different cases; sometimes the teeth diverge, and at others they slant towards each other. Fig. 2 illustrates a good example of the deformity. In any case in which the malformation was as marked as in this sketch, I should feel no hesitation in pronouncing the possessor of the teeth to be the subject of inherited syphilis even in the absence of other testimony. I have never yet seen such teeth excepting in patients of this class. In the majority of cases, however, the condition of the teeth is sufficient only to excite suspicion and not to decide the question. In a few rare cases only one of the upper central incisors is malformed, the other being of natural shape and size. A good instance of this state of things is shown in Fig. 3.

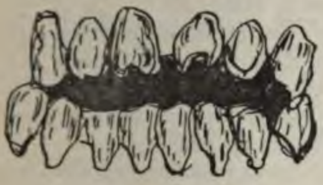

FIG. 2.

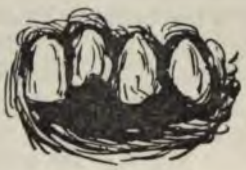

FIG. 3.

In a considerable number of cases of heredito-syphilis the teeth show no deviation whatever from the normal standard, and in such the diagnosis must be guided by other conditions. In addition to the peculiar malformations above described and illustrated, there are others which, although less characteristic, are yet very valuable to a trained observer. They do not, however, admit of description without great risk of misleading the reader. Before leaving the subject of dental malformations I may again draw attention to the fact that it is only in the permanent set that any peculiarities are observed. The first set are liable to premature decay, but are not malformed.

In addition to the peculiarities of physiognomy and the malformations of the teeth, the diagnosis may be much helped by observing the state of the eyes and of the bones. If there be evidences of past iritis, or if there be clouds in the substance of the corneas, the results of past keratitis, or especially if the corneas be now attacked by this peculiar inflammation in its acute stage, very valuable evidence will have been obtained. The phenomena of syphilitic keratitis in its acute stage are peculiar and easily recognised. Both eyes are usually affected at the same time. The corneal tissue becomes very extensively opaque by the effusion of lymph into its substance; its tint may vary from that of ground glass to a red salmon colour. There are no ulcers in its surface. A zone of ciliary congestion is usually well marked. Whilst the disease is at its height the patient is often practically blind for several months. The intolerance of light is usually considerable. After the inflammation has passed away the cornea usually clears in a most remarkable manner, but it rarely regains such perfect transparency that the experienced observer cannot detect traces of what has taken place. These traces consist in a somewhat dusky and thin sclerotic in the ciliary region, and in the presence of slight clouds here and there in the corneal substance, there being no scars in its surface. The difference between these interstitial clouds and ordinary leucoma is easily observed.

In a few cases the existence of nodes on various long bones may help us to a diagnosis; in others we may obtain aid from finding that the patient has become deaf without otorrhœa, or that he is partially blind from choroiditis. What are known as Parrot's bosses are low elevations on the parietal eminences caused by infantile periostitis.

With regard to the general arrest of development in heredito-syphilis, I may remark that it is a very untrustworthy indication. In a few cases this taint dwarfs the whole body in a most remarkable manner, but in most cases no retardation of general growth is observable. A pale complexion is almost always met with. It is exceedingly rare to meet with a good florid complexion in a young adult who is the subject of this taint. We do, however, every now and then see a physiognomy which neither in shape of features nor in colour of cheeks and lips furnishes the slightest clue. I have met with arrest of sexual development in one or two instances. In one of these, a young woman who was under the care of Dr. Hughlings Jackson in the London Hospital, there was such an entire absence of all sexual characteristics, that I could not but suspect that the ovaries had been destroyed by syphilitic inflammation in early life.

CONTRASTED PARALLEL BETWEEN THE COURSE OF SYMPTOMS IN ACQUIRED AND INHERITED SYPHILIS

I have endeavoured in the following tabular statement to compare as clearly as I can the resemblances and differences in the course of symptoms when arising from acquired or from inherited taint. To some of these I have already incidentally alluded, and respecting the others the statements in the table will, I trust, explain themselves :—

ACQUIRED DISEASE

Primary Stage.—Local or stage of inoculation. The sore, which may have been present almost from the first, does not assume characteristic features till the end of a month. It may remain for a fortnight to six months.	An ulcer (chancre) usually with indurated base. Indurated lymphatic glands. Induration is to be regarded as the earliest proof of successful inoculation, but it is not infrequently absent throughout.
Secondary Stage.—Constitutional or exanthematous. Usually commence within six weeks or two months of the inoculation, and if not treated, may last from three to six months or to a year. Essentially transitory, and will disappear without treatment.	Febrile disturbance, malaise and muscular pains. Slight engorgement of lymphatic glands in many parts. A symmetrical and usually copious eruption on the skin, and often on exposed mucous surfaces. Symmetrical ulcers in tonsils. Iritis, retinitis, etc., usually symmetrical. Loss of hair, loss of flesh and of strength. This stage may be either exceedingly slight or very severe. Its severity appears to bear proportion to the degree of induration of the preceding chancre. It is often noticed that the rash comes out in successive crops. The rash may also vary very widely as to its character, roseolous, scaly, papular, pustular, ecthymatous, etc., being modified probably by peculiarity—first, in the source of contagion; secondly, in the idiosyncrasy of the recipient. The whole of the arterial and capillary system may suffer.
Intermediate Stage.—Stage of latency and of relapses. This stage may be said to commence at from a year to a year and a half after the contagion, and to extend over a period which may vary from three to five, ten, or even twenty years. It passes insensibly into the tertiary stage.	The patient may be either wholly free from symptoms and in good health, or he may remain pale and rather feeble, and liable from time to time to slight returns of eruption on the skin, sores on the mucous membranes, condylomas, etc. The arterial system is still liable to be affected and various forms of paralysis may result. He is protected as regards fresh contagion, and should he beget children they are very likely to suffer. The relapses during this stage are usually easy to be distinguished from true secondary symptoms. There is little or no febrile disturbance, the rash is not copious, and often not symmetrical. Acute iritis, retinitis, etc., never occur; that is, they do not occur for the first time, though they may in the form of relapses.

Tertiary Stage, or stage of sequels.

This stage commences at from four to ten or to twenty years after the contagion, and extends indefinitely, occasionally to the end of life.

All the symptoms in this stage occur, as a rule, without symmetry; sometimes multiple, but not infrequently single. They consist of chronic inflammations of deep tissues, or of the deeper layers of superficial ones, for example—inflammations of periosteum and bone resulting in nodes; of cellular tissue, tendon, or muscle, resulting in gummy tumours; ulcerative destruction of the palate and pharynx; serpiginous ulcerations of the skin; inflammations of nerves, or even of cerebro-spinal centres, inducing various forms of paralysis; deposits in liver, lungs, etc. Diseases of the arterial system are now less common. Probably but little liability to transmit the disease to offspring. Protection against a new contagion incomplete. All the inflammations in this stage are remarkably under the influence of treatment by iodide of potassium, but tend to relapse. Unless so treated, all of them tend to progression and permanent disorganisation of the part attacked, none of them to spontaneous recovery.

INHERITED DISEASE

Primary Stage.

The infants usually remain without symptoms for from one week to three months.

This stage has been passed through by one or both of the sufferer's parents within from a few months to several years before the infant's birth. The infant is usually free from all symptoms at the time of birth.

Secondary Stage.—Constitutional or exanthematous.

From the age of two to four weeks to the end of the first year.

This stage is essentially transitory, and will disappear without treatment, if the child lives.

Inflammation of nasal mucous membrane causing "snuffles."

A symmetrical and usually copious eruption on the skin. Wasting; fretfulness; a peculiar odour; a withered, senile aspect; inflammation of the mouth, and condylomas at anus; iritis, usually symmetrical; arachnitis and slight effusion; disease of liver (rare); nodes (very rare). Periostitis of the skull bones frequently occurs symmetrically. The eruptions which occur differ from those of acquired disease, chiefly in being more moist, and in preferring the thighs and genitals. These differences may in part be due to peculiarities in the skin of young infants, and to the constant irritation from urine to which the nates are liable. Dry scaly rashes are rare. Iritis is much less frequent than in the adult, but just as well characterised when it does occur.

In infants this stage often proves fatal.

ntermediate Stage.—Stage of latency.

This stage extends from the end of the first year or eighteen months to the second dentition, the time of puberty, or even very much later.

The patient will probably be wholly free from active symptoms, but will show various indications of his diathesis in pallor of skin, sunken nose, protuberant forehead and premature loss of the upper incisor teeth. Sometimes there will be a remarkable retardation of growth and general development. If second dentition have occurred, the central upper incisors will be malformed. Unlike what happens during this stage in acquired syphilis, we scarcely ever observe any tendency to recurrence of the secondary symptoms. Now and then we see condylomas at the anus returning during the first five years, but the rash of infantile syphilis having once disappeared, scarcely ever relapses. A certain degree of nasal obstruction sometimes persists, but not often.

Tertiary Stage, or stage of sequels.

This stage may commence with the second dentition, at the time of puberty, or not till much later. Its duration is quite indefinite.

Most of its symptoms are symmetrical:—

Keratitis (interstitial); kerato-iritis; periosteal nodes; deafness (not infrequent); blindness (rare); disease of liver and kidneys; phagedænic or serpiginous ulcerations of skin; cellular nodes (rare). Probably not liable to transmit the disease to offspring. Protection against a new contagion incomplete. The symmetry of the symptoms is in marked contrast with what occurs in this stage of acquired disease. The paralysis of single cranial or spinal nerves, so common from acquired syphilis, are seldom met with in the inherited form.

Most of the inflammations tend, unless arrested by treatment, to permanent disorganisation, but one (interstitial keratitis) tends to recovery even without treatment. They are much less easily influenced by treatment than those of the acquired disease. Disease of the arterial system and its consequences, so common in acquired syphilis, is very seldom seen in the subjects of inherited taint.

JONATHAN HUTCHINSON.

COEXISTENCE OF INFECTIOUS DISEASES

The fact that two or more infectious diseases are capable of running concurrently in the same individual is not so generally recognised as the frequency of its occurrence would warrant.

Hunter even went so far as to deny the possibility of such coexistence, and to his teaching must doubtless be ascribed the wide currency to which this belief has attained. Murchison in 1859, while reporting cases in point, asserted that the prevalent opinion was opposed to the possibilities of any such coexistence, though he himself was fully alive to the truth.

Now it is universally admitted that the convalescent stage of many and various infectious disorders is not infrequently interrupted by the appearance of a second; and it is within the experience of those who are daily concerned in dealing with large numbers of cases of the infectious fevers, to find two such diseases running concurrently, and in exceptional instances three (3) or even four (4).

So far from coexistence being an impossibility, clinical experience would tend to show that the presence of one disease in the body increases the liability to the infection of another. The susceptibility not only varies in respect to different diseases, but is usually increased in proportion to the severity of the primary attack.

Any inference, drawn from a simple statement of figures, as to the relative susceptibility evinced by the subjects of a particular disease in respect to the development of any particular second, is unfortunately vitiated by the fact that the liability to contract a disease varies with the chances of exposure to its infection. The varying influences of season, local prevalence, relative isolation, the protection conferred by a previous attack, and other factors, must all be discounted in addition to the varying susceptibility seen in connection with age.

I. The following list specifies the number of attacks amongst 48,366 consecutive cases of scarlet fever treated in the hospitals of the Metropolitan Asylums Board which were complicated, either during the acute stage or during convalescence, by the appearance of a second infectious disorder (5).

In	1094	cases	the secondary	disease was	Diphtheria.
,,	899	,,	,,	,,	Chicken-pox.
,,	703	,,	,,	,,	Measles.
,,	404	,,	,,	,,	Whooping-cough.
,,	55	,,	,,	,,	Erysipelas.
,,	11	,,	,,	,,	Enteric fever.
,,	1	,,	,,	,,	Typhus.

Now, for the reasons above stated, the foregoing numbers cannot be taken as an accurate expression of the proportionate liability to coexistence; moreover, in a considerable number of these cases the complicating disease did not appear until late convalescence: yet the figures are not without a certain rough value.

Experience shows that the diseases which most frequently complicate *scarlet fever* are *diphtheria*, *chicken-pox*, and *measles*, and that *whooping-cough* comes next in frequency, especially in very young children.

Although post-scarlatinal diphtheria is a well-recognised condition, much confusion exists at the present time in respect to those cases of *scarlet fever* which are complicated with *diphtheria* during the acute stage.

Seeing that in many cases of simple scarlet fever an exudation is found on the fauces, which is not diphtheria closely as it may simulate it, the mistake is often made of adopting too wide a generalisation, and of referring all "exudation throats" to the same category; thus virtually ignoring the possibility of the coexistence of diphtheria with scarlet fever in the acute stage.

In the large majority of cases in which diphtheria is found to complicate scarlet fever, it arises during the convalescent stage of the scarlatinal attack; in which case the infections, as living processes, are not strictly coexistent. It must also be conceded that by far the greater number of faucial exudations seen during the acute stage of scarlet fever are not examples of coexistent diphtheria, but are simply dependent upon the intensity of the tonsillitis associated with certain micro-organisms which are commonly present in the scarlatinal throat.

That *measles* and *chicken-pox* should frequently be found to arise in children suffering from scarlet fever is only what might be expected in view of the high degree of infectivity possessed by these disorders; moreover the age incidence in the three diseases is in close agreement.

There is little doubt that many more instances of coexistent *whooping-cough* would have to be recorded were the age incidence in the two diseases more equal. The maximum susceptibility to whooping-cough would appear to be during the second, third, and fourth years of life; whereas in scarlet fever the greatest liability is evinced during the fifth and sixth years.

That *scarlet fever* patients are but little prone to *enteric fever* is evinced by the fact that only eleven instances are recorded in 48,366 attacks.

This inference is supported by a statement of Murchison, that in the course of twenty-three years' experience at the London Fever Hospital, at a time, too, when all classes of disease were treated in the same wards, and many thousand cases of scarlet fever were admitted, not more than eight instances were recorded in which the scarlet and enteric fevers were coexistent (6). Here, again, the age incidence in the two diseases being widely different, the relative susceptibility would naturally not be very great. If it were, the similarity in the curves of their seasonal prevalence would doubtless tend to increase the chance of their occasional coexistence.

That *typhus* is capable of existing with *scarlet fever* is attested by Murchison (6). At the present day the opportunity of observing their coexistence must necessarily be rare. The only case which has come under my own notice was that of a boy aged eight, in whom the typhus eruption appeared on the third day of a typical attack of scarlet fever. The severity of the combined attack was too great for the child, and he died on the fifth day after the eruption came out. In this case the typhus was, no doubt, contracted first.

As in the converse instance, but possibly to a less degree, the *diphtheria* patient is very liable to take the infection of *scarlet fever*, and this susceptibility is certainly as well marked in the acute stage as it is in later convalescence. That in both diseases the faucial mucous membrane is the part first and mainly affected, is very suggestive of this part being in each case the point at which infection is received. As regards diphtheria modern research and clinical observation have confirmed this view beyond all reasonable doubt; the mucous membrane of the throat, weakened by the scarlatinal inflammation, provides a soil most favourable to the development of the Klebs-Löffler bacillus. Whether the reverse hold good, namely, that a mucous membrane, either at the time, or previously, affected with diphtheria, is thereby rendered more susceptible to the virus of scarlet fever, is not so certain. The rapid spread of scarlet fever amongst the inmates of a diphtheria ward, if once it gain admission, and its preference for the severer cases, are matters of common observation; moreover, the fact that, in many cases of scarlet fever, a sore throat precedes, by a week or more, the symptoms of definite invasion, is very suggestive of such being the case.

It is not uncommon for *diphtheria* patients to be attacked with *measles*, *chicken-pox*, and *whooping-cough* (7), but there is nothing to point to any special susceptibility in respect to any of these diseases.

The subjects of *measles*, though they may develop any of the other infectious disorders, evince a special susceptibility to *diphtheria* and *whooping-cough*. The gravity of the former complication is extreme, as both the diseases almost always affect the respiratory passages. In respect to whooping-cough the liability lasts for some weeks after obvious catarrh has ceased.

There would, therefore, seem to be a correlated susceptibility in respect to measles and whooping-cough such as appears to exist between scarlet fever and diphtheria.

The actual concurrence of *small-pox* and *scarlet fever* is not very common, although the small-pox convalescent is very liable to take scarlet fever if exposed to its infection. *Erysipelas* again arises not infrequently in confluent cases.

II. Now, as concerns any modification of the characters of one disease in virtue of the coexistence within the body of another, it may be stated that there is no evidence to warrant the belief that the incubation stage of either is interfered with in any particular.

Just as the latent period of independent chicken-pox, measles, or small-pox is more constant than it is in independent attacks of scarlet fever, diphtheria, and enteric fever, so it is when either of them occurs as an intercurrent affection during the progress of another disease. A primary vaccination runs precisely the same course in a scarlatinal child as it does in a healthy infant.

Until it is established experimentally that an antitoxine or protective proteid, resulting from the growth of any one pathogenetic microbe in man, is capable of either inhibiting the growth of another, or of neutralising its poison, there would be no *prima facie* reason to expect the products of one organism to be capable of modifying the development of another in a medium so eminently favourable to growth as is afforded by the human body; unless the poison be present in overwhelming quantity. The restraining influence of certain putrefactive organisms is, however, admitted.

It may then be affirmed generally, that the symptoms of one disease are neither delayed in their appearance, nor mitigated in their severity, by the presence of another; but that the characteristics of each are for the most part well defined, and in some instances even exaggerated.

The gravity of the combined manifestation would seem not to vary so much with the severity of the primary attack, which seems to have more effect in determining susceptibility, as with the propinquity in the incidence of the two disorders.

There are, nevertheless, clinical points characterising the conjunction of certain members of the infectious group which are deserving of mention.

When *diphtheria* arises during the acute stage of *scarlet fever* the patient's condition is usually very grave, apart from the chance of extension to the larynx. There is a great liability to mistake a non-diphtheritic scarlatinal exudation, or the surface necrosis (*scharlach nekrose* of Professor Henoch) which is sometimes seen on the tonsils in severe cases of scarlet fever, for the state in which both diseases are present. The following points may assist in discriminating the two conditions:—The scarlatinal exudation is usually limited to the tonsils; it is apparently dependent upon the intensity of the associated tonsillitis; the surrounding mucous membrane is usually of a dark, angry tint, and frequently presents a somewhat dry and sticky appearance; the exudation itself either consists of a thin pellicle, which is easily detached, and commonly disappears in a day or two, or it is represented simply by a necrotic surface on the tonsil. This soon proceeds to ulceration with a grayish white, woolly-looking surface which may extend both superficially and in depth, and ultimately lead to extensive destruction of the faucial tissues. At all stages of this condition the streptococcus pyogenes, the pus staphylococci, and numerous putrefactive bacteria are usually to be found in abundance; but the Klebs-Löffler bacillus is conspicuous by its absence, whether sought for in the recent exudation, or by careful cultivation in suitable media; and the attack will not be followed by paralysis. In coexistent diphtheria, on the other hand, the exudation more frequently invades the palate, uvula, and the pillars of the fauces; it is usually thicker, especially at the margin, and for a time more adherent; it bears no relation to the intensity of the tonsillitis, and the mucous membrane is often comparatively pale, of a pinkish tint, and usually presents a glairy appearance. The constitutional depression is more profound at an earlier date than is usual in scarlet fever. The Klebs-Löffler bacillus can be isolated with ease in practically all cases, together with certain pyogenetic bacteria, notably streptococcus pyogenes and staphylococcus albus; moreover, some degree of paralysis is found at a later stage in a large proportion of patients who survive.

The bacteriological test, and the occurrence of post-diphtheritic paralysis, are by far the most valuable criteria of the presence of coexistent diphtheria; and I have often found the Klebs-Löffler bacillus in cases in which a definite diagnosis could not have been otherwise obtained. The large majority of such cases are fatal; and the reason why diphtheritic paralysis is not more frequently observed is that the patients usually die before the advent of this sequel.

Diphtheria of convalescence, or *post-scarlatinal diphtheria*, is dealt with in the section devoted to scarlet fever (p. 159).

When scarlet fever arises in a patient who has recently suffered from diphtheria, that is, during the first few weeks of the illness, a recrudescence of diphtheritic membrane frequently occurs; although the fauces may have been clear for the previous two or three weeks. The development is interesting as exemplifying a recrudescence of vitality on the part of a microbe in response to a change in its environment. The process, however, is rarely characterised by excessive virulence.

When *chicken-pox* complicates the *scarlatinal attack*, either during the eruptive stage or during convalescence, the attacks are on the whole more severe than in the independent disorder. The eruption is usually more copious, and there is possibly a greater tendency to pustulation. In cases in which the eruptions are coincident, the varicella will have been contracted at an earlier date than its fellow.

It is not very common to find *measles* actually coexistent with *scarlet fever*, although either is frequently to be met with during convalescence from the other. In the former case the diagnosis may present some difficulty, as the combined eruption will present some special features of both diseases. The eruption is usually intense, often patchy in distribution, and generally invades the circumoral region. A *mottled* staining remains behind after the rash has faded, often associated with free desquamation; a conjunction which is not met with in any single infectious disease. If the eruptions are nearly coincident, the rapid fall of temperature, which in most cases of ordinary measles takes place within forty-eight hours of the appearance of the rash, may be arrested by the longer sustained pyrexia of scarlet fever, and may thus be quite devoid of its usual characters.

Ulcerative stomatitis is very prone to appear in such cases, occasionally running on to definite noma, and there is a marked tendency for the bronchial catarrh to develop into serious lung mischief.

It is a curious fact that the eruption in post-scarlatinal measles often appears earlier than in the independent disease. In seventy-eight consecutive cases of measles arising in scarlatinal convalescents the eruption was delayed until after the third day in four instances only. In a large majority it appeared on either the first or second day; and in a considerable number it was the first sign of illness. These were cases of undoubted measles, not of rötheln.

Post-scarlatinal measles is a serious combination, the mortality in this series being over 14 per cent.

The appearance of a suffocative cough, attended with progressive laryngeal stridor, usually implies the presence of membrane in the air-passages. This, in some cases at any rate, is true diphtheria.

When *measles*, as the primary disease, is complicated with definite *diphtheria*, either during the eruptive stage or later, the condition is one of extreme danger in view of the constancy with which the latter disease affects the larynx and respiratory tract. It constitutes the most serious conjunction of any two infectious diseases. The fatality is not only increased in virtue of the malignant type which the disease assumes, but the persistence with which the membrane reforms, if successfully expelled, renders the case well-nigh hopeless. Tracheotomy is very rarely successful, but the effects of antitoxine seem most encouraging.

When *measles* occurs in a patient who is suffering from *whooping-cough*, the tendency to the development of capillary bronchitis and broncho-pneumonia is thereby greatly increased. The fatality, as might be expected, is in inverse proportion to the age of the patient.

It is a curious fact that when the course of *whooping-cough* is interrupted by an intercurrent attack of *scarlet fever*, the characteristic "whoop" is often entirely dropped during the febrile stage of the latter affection, but returns when the temperature has again become normal.

The same phenomenon is occasionally observed during an attack of intercurrent measles.

A child once came under my care in whom *scarlet fever*, *diphtheria*, *measles*, and *whooping-cough* were all present at the same time, the only disease amongst them in which the diagnosis was doubtful being diphtheria, for the bacteriological test was not applied. In another case the eruptions of *measles* and *chicken-pox* were mingled with the early desquamation of *scarlet fever* in a child who at the time was suffering from *whooping-cough*. In both cases the combined attack was fatal.

For instances of cases of enteric fever mixed with other infections, the reader is referred to the subsection on "Mixed Infection" in the article on Enteric Fever in this *System* [vol. i. p. 832].

Instances in which the course of one infectious disease has been complicated by the appearance of a second have been recorded by many competent observers during the last fifty years; and such concurrences may be frequently observed in the wards of any large fever hospital.

F. FOORD CAIGER.

INCIDENTAL RASHES.—The suspicions of the physician may be aroused, or his diagnosis rendered uncertain, either by the appearance of accidental rashes in the course of febrile diseases, or by their unexpected occurrence at other times. Rashes due to drugs, for example, may disconcert even an experienced observer. This matter could not well be inserted in this place, and the reader is referred to a chapter upon it by Mr. Jonathan Hutchinson, Junior, which will be published in the section on Skin Diseases.—ED.

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F. F. C.

DISEASES OF UNCERTAIN BACTERIOLOGY

(*b*) TOPICAL OR ENDEMIC

(FEVERS OF INDIA)
26. TYPHUS FEVER
27. DENGUE
28. YELLOW FEVER
29. DYSENTERY
30. BERIBERI
31. MALTA FEVER
32. EPIDEMIC DROPSY
33. NEGRO LETHARGY
34. DELHI BOIL
35. VERRUGA
36. FRAMBŒSIA

ON THE CLIMATE AND SOME OF THE FEVERS OF INDIA[1]

SECTION I.—CLIMATE

BEFORE describing the fevers of India, it is expedient to give a brief account of the geographical position and physical and meteorological characters which are important factors in determining the climate, and the conditions of disease in that country.

The Indian Empire, including Burmah and the Shan States, is situated between the 66th and 104th meridians of east longitude, and the 8th (or 6th including Ceylon) and 35th parallels of north latitude; it exceeds a million and a half square miles in extent, and is contained within a coast-line of (approximately) 4600 miles, and a land boundary of over 5000 miles. India proper is a vast triangle, the apex of which is at Cape Comorin and the base at the Himalayas. Its extreme length from Cape Comorin to Peshawar is about 1900 miles, whilst its greatest breadth near the base, from Baluchistan to Assam, is over 2000 miles.

The geographical position of this vast promontory, with the Bay of Bengal on the east and the Arabian Sea on the west, a great part lying within the torrid, the rest within the temperate zone, its physical characters, comprising lofty mountain ranges rising in the north to the abodes of eternal snow, extensive forest tracts, jungles and swamps, noble rivers and estuaries, vast plains formed by their basins and deltas, elevated plateaus and arid deserts, invest it with peculiar interest for those who would study the physical and climatic conditions which govern the progress and welfare of the human race and the origin and characters of disease.

The natural divisions of India are:—

1. The Himalayan and Sub-Himalayan region.
2. The Indo-Gangetic basin and deltas.
3. The peninsula proper formed by the plateau of the Deccan, bounded on each side by the Ghâts and the littorals lying between them and the ocean.
4. To these must be added the provinces of Lower and Upper Burmah.

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[1] The spelling of the names is in accordance with that of Sir W. W. Hunter's *Gazetteer of India*, except those in the tables, which are copied from the *Report of the Sanitary Commissioner with the Army of India*.

1. *The Himalayas* extend south-east and north-west in a double crescentic range for nearly 1750 miles, with a breadth of from 150 to 250 miles. Their mean height is from 16,000 to 20,000 feet; the highest points are Kinchinjunga (28,176 feet) and Everest (29,002 feet). The Sub-Himalayan region consists of two ranges, separated by a broad valley (the Dun), and bounded on the south by the belt of pestilential forest and swamp land called the Tarai. The Himalayan provinces are Bhotan, Nepál, Gharwál and Kashmir.

2. *The Indo-Gangetic plain*, or Hindostan proper, which separates Peninsular India from the Himalayan region on the north, the Sulaiman and Khirtar ranges on the west, and the hill regions of Assam, Chittagong, and Tipperah on the east, has an area of 300,000 square miles, and a breadth varying from 90 to nearly 300 miles; it forms the richest and most populous part of the Empire. The rivers with their tributaries which water this plain are the Indus (length over 1800 miles), the Ganges (length 1557 miles), and the Brahmaputra, over 600 miles of which lies within British territory. The delta of the Ganges and Brahmaputra forms an irregular parallelogram of alluvium of about 50,000 square miles. The water-parting of the Indus and Ganges is about 900 feet above sea-level; the slope especially towards the east is very gradual. The provinces included in this region are Bengal, Assam, North-Western Provinces, Oudh, the Punjab, Sind, Rajputana, and other feudatory states.

3. The third natural division, *Tropical or Peninsular India*, is bounded on the north by the Vindhyas, consisting of various ranges from 1500 to 4000 feet high, which extend for nearly 800 miles from east to west, including the Aravalli and Satpura ranges; at their extreme west is Mount Abu (Aravallis), 5653 feet high; in the east Parasnath, 4479 feet high. The Eastern Ghâts, a less continuous series of hills, forming rather a descent from the plateau to the littoral than a distinct mountain range, extend along part of the east coast, with an average elevation of 1500 feet, having broad tracts of level ground between them and the ocean. The Western Ghâts extend from the Vindhyas, down the coast, with an average height of about 3000 feet, but much nearer the sea than the Eastern Ghâts. In the south, where the two systems join, an elevation of over 8000 feet is reached.

The Deccan plateau, enclosed between these three ranges, slopes gradually to the east, and has an elevation varying from 1000 to 3000 feet; it is, broadly speaking, a region of wide open valleys and easy slopes, with isolated peaks here and there, and ranges of hills, of which the most important are the Nilgiris, whose highest point is Dodabetta (8760 feet).

The provinces included in Peninsular India are the Central Provinces, Berar, Madras, Bombay, Mysore, with the territories of the Nizam, Sindhia, Holkar, and other feudatory states.

There are two great slopes of drainage, into the Bay of Bengal on one side and the Arabian Sea on the other; the water-parting extends nearly vertically from Kashmir to Cape Comorin. The Arabian Sea receives the Indus, Narbada, Tapti, and the rivers that water the narrow plain between the Western Ghâts and the sea; the Bay of Bengal receives the Brahmaputra, Ganges, Mahanadi, Godavari, Kâveri, Kistna, and others of less importance.

There are few natural fresh-water lakes in Peninsular India, but artificial reservoirs are many. In the Himalayas there are several lakes at elevations of from 4000 to 6000 feet: salt lakes formed by lagoons and inlets of the sea are found along the east coast, as the Pulicat, Chilka and Kolár lakes; and along the west coast, as the Runn of Cutch. There are also inland salt lakes, such as Sambhar in Rajputana, and Lonár in Berar. These are interesting physical features, but they have no very marked influence on climate.

The island of Ceylon (length 270 miles, breadth 157 miles), like Peninsular India, has a belt of low land round its coast formed of tertiary strata. There are numerous lagoons on the east coast; the mountain system reaches an elevation of 8280 feet. Numerous rivers fall into the sea on the east and west coasts, and their basins and the sides of the hills and sea-coast are the seats of dense tropical vegetation. The climate on the sea-coast is equable, though the temperature is high and the atmosphere humid.

4. *The Province of Lower Burma* (area, 87,220 square miles) consists (i.) of the belt of alluvial plain stretching along the eastern shore of the Bay of Bengal, and bounded on the east by the forest-clad ranges of the Yoma mountains, whose highest point is over 7000 feet; (ii.) the lower course and delta of the Irawadi and Sittaung, the most productive part of the whole province; (iii.) the narrow strip of land, Tenasserim, consisting of low land along the coast, succeeded farther inland by hill country, intersected by many streams. The Salwin is the main river of this district. There are three distinct mountain systems—the Arakan and Pegu, Yoma, and the Paunglaung, of which the Tenasserim Hills may be regarded as a continuation. Forest districts are extensive, covering an area of about 50,000 square miles.

The climate is warm but equable.

Upper Burma (area, 190,000 square miles), which is altogether inland, is in the main an upland country with isolated tracts of alluvial plain. It is watered by the Irawadi and the Salwin and their tributaries. For about 300 miles from its western frontier the country is undulating, with occasional ranges of hills; beyond it is wild and mountainous. Some districts are intensely malarial.

The Indian Empire, which nearly equals in size the whole of Europe excluding Russia, and whose population consists of over 289,000,000 (about a fifth of that of the world), presents many and great differences of race, religion, manners, customs, physique, language and disease.

It is necessary to say a few words on the geology, climatology, ethnology, and sociology of this vast country.

The great northern Himalayan area is a region of mountains, deep-cut valleys, and steep hill-sides. The range south of Tibet consists of (i.) the zone of the snowy peaks and Lower Himalayas, composed of crystalline and metamorphic, gneissic and granitic rocks, which have undergone upheaval probably about the close of the secondary or beginning of the tertiary period, and of unfossiliferous sedimentary beds believed to be principally of palæozoic age, with nummulitic limestone found occasionally at an elevation of 20,000 feet; (ii.) the zone of the Sub-Himalayas, which consist largely of later tertiary deposits, as in the Siwaliks, and contain extensive fossil remains of an extinct mammalian fauna.

In the north-west the hills between the Jehlam and the Indus form the salt range, containing vast beds of salt and stratified rocks of almost every geological epoch. It is said to have formed at one period part of the southern limit of the Asiatic mainland.

Along the foot of the Siwaliks lies the Bhaber, a forest belt on sloping, gravelly soil. Through this the water percolates to a bed of clay, which brings it to the surface on the edge of the alluvial plain; here it gives rise to a densely-wooded, damp, pestilential tract of an average breadth of twelve miles, known as the Tarai, which stretches from the Ganges along the foot of the Himalayas to Assam. The vegetation covering the sides of the lower ranges of the Himalayas influences the amount of rainfall, and modifies its distribution in the soil as it enters the alluvium at the base of the hills.

The alluvial tract of the Indo-Gangetic plain, stretching across the north of the peninsula, is drained by the rivers that flow from the Himalayas, and traverse it in channels which are cut more or less deeply below its general surface. Borings made at different localities across the plain have shown that the alluvium has a depth of many hundreds of feet.

There are valleys in Assam and Cachar which appear to have undergone depression at a recent geological period. They contain large swampy regions which are subject to flooding when the rivers are full. Where these rivers enter the Bay of Bengal we find, along the sea-face of great part of the delta, a broad pestilential zone of swampy land thickly covered by low jungle, known as the Sundarbans.

The peninsula of India is mainly composed of various forms of gneissose, granitoid and allied rocks; the general character of the newer rocks which rest upon them is silicious and sedimentary, with the exception of the great series of volcanic rocks which occupies all the western portion of the peninsula, from the west coast north of Malwa eastwards to Nagpur. There is a great tract of almost treeless country covered in part by the fertile cotton soil, in part by barren laterite, in part by flat-topped hills of volcanic rocks. From the eastern flanks of the Aravalli mountains there stretches a great region of sandstones, shales and limestones, as also notably in the Vindhyan range.

There are no evidences of recent volcanic action on the peninsula, but Barren Island, in the Bay of Bengal, bears evidence of comparatively recent activity. In some parts of Burma, and also in Baluchistan, there are so-called mud volcanoes which discharge gas, mud, and small quantities of petroleum, and appear to be referable to the causes which give rise to hot springs found in different parts of India; some yield pure water, as Sita Kund, near Monghyr, others water impregnated with various saline matters.

With reference to the nature of the soil and the subjacent water—a matter of great importance—it is to be noted that rain-water takes up in solution more or less mineral matter derived from the decomposition of the rocks. This consists principally of carbonates of the alkaline earths, chiefly lime, which give rise to the formation of that peculiar nodular calcareous concrete known as kunkar, and of chlorides and sulphates of the alkalis, principally soda (*reh*).

In alluvial tracts, where the soil is formed of partially decomposed rock, the production of soluble salts is great; well waters there contain proportions of these salts varying from 30 grains per gallon to 300 grains or more. In the plains of Upper India, where the production of soluble salts is rapid, and the subsoil water rises to near the surface, these salts occasionally crystallise out on the surface, in consequence of the excessive evaporation; thus a crust is produced which, effectually preventing vegetation, sterilises large tracts of land; and the impregnation of the well waters may have a deleterious effect upon health. Considerable areas of different parts of the land surface, especially in the vicinity of old villages, are the seat of nitrification.

The geographical and physical characters above mentioned involve **varieties of climate,** and between Northern and Tropical India, according to latitude, elevation, and other physical attributes, every degree of difference in temperature or humidity is found. Milton's description of a trying climate is amply illustrated in India :—

> For Hot, Cold, Moist and Dry, four champions fierce,
> Strive here for mast'ry, and to battle bring
> Their embryon atoms.
>
> *Paradise Lost.*

There are three distinct seasons in India—the hot, the rainy, and the cold—which vary in duration and in times of setting in, transition from one to the other being somewhat gradual; approximately, the cold season extends from November to March, the hot from March to June or July, and the rainy season from that to October, these seasons being greatly influenced by the monsoons.

In the beginning of April, when the whole surface of the continent becomes hotter than the sea, the rarefied air rises and is replaced by the cooler currents drawn in, laden with moisture, from the Indian Ocean. This is the south-west monsoon, which, commencing with storms of thunder and wind, bursts in rain on the Malabar coast, rises to higher regions, and, being intercepted by the mountain ranges, condenses its moisture in heavy rain on the Western Ghâts and on the coast of Arakan. Following a north-eastern course it gradually loses its force, which is much diminished ere it pass the 25th parallel of north latitude. The Carnatic and Coromandel coasts, being sheltered by the Western Ghâts, are comparatively dry when the west coast is deluged with rain.

About October the winds are variable; there is a reversal of the current, which blows southwards for the most part as a dry wind, till it brings moisture from the Bay of Bengal, which falls as rain on the coast of the Carnatic and on the Eastern Ghâts; whilst some parts of the South of India receive a certain amount of rain with each monsoon.

On the western coasts the rainfall is the heaviest; but there are many local variations, some elevated regions receiving almost a deluge, whilst other lower areas are comparatively dry. The conditions favourable to condensation and fall of rain concur in certain localities, whilst the reverse obtains in others. The climate varies accordingly; in the plains of Hindustan and the tablelands of the Deccan the heat is intense and dry, though often, as in Bengal, it is greatly modified by moisture. In the south, where the diurnal and annual range of temperature is comparatively small, the sea-coast enjoys a fairly equable, though warm and humid climate; but all along the coast the heat is tempered by sea-breezes. In the north-west the changes of temperature are often great and sudden. In the cold season the heat in the day may be great, but the temperature at night may fall some degrees below freezing-point.

The effects of a dry or moist atmosphere at the same temperature are very different. Dry air in motion at a temperature of 100° is more tolerable than stagnant air laden with moisture at 80°. The hot, dry winds of some parts of the Deccan and Northern India, which blow during the months of May and June, are more endurable than the cooler but humid atmosphere of Lower Bengal, of parts of Southern India, or even the arid tracts of Sind; there, though there be very little rain, the atmosphere is humid.

In the north-west the rains begin towards the end of June, and fall in diminished quantity. In the Punjab, near the hills, the rainfall again increases, but in the Southern Punjab and in the great desert regions there is very little rain, in some parts none. In the north-east corner of India the wind that brings the rain blows over the Bay of Bengal from the south-east; and from this quarter Bengal and the Gangetic valley receive their rain.

The north-east monsoon commences gradually in October, and is attended with dry weather throughout the peninsula generally, except on the Coromandel coast where it brings rain from the Bay of Bengal between October and December. A little rain frequently falls in December in Bengal and other parts in the north, after which it is dry until March, when variable winds set in which last till about June, when the heat is great. About the end of May the south-west monsoon again sets in, bringing a few showers known as the lesser rains. In the hill stations, such as Darjiling, Masuri, Naini Tal, Marri, Chakráta, Simla, and generally in the elevated stations of the lower ranges of the Himalayas, also at Utakamand, Kunúr, Wellington, in the Nilgiris—stations at elevations of 5000 to 7000 feet—the climate is genial; it is cool and healthy in summer, and almost as bracing in winter as Europe. The rainfalls of the southern hill stations, such as Utakamand and Wellington, are 46 in. and 48 in. in the year; whilst in the Himalayan stations it is heavier, being at Simla 70·3 in., at Chakráta 61 in., at Marri 56 in., and at Darjiling 127: the latter, however, is quite an exceptional rainfall. Objections are sometimes made to the hill stations on account of dampness, owing to the quantity and duration of the rainfall; but withal the hills are justly favourite health resorts, and may perhaps become the sites of colonisation.

In the north-west of India some regions have a rainfall of less than 15 inches; in many parts of it much less, even as little as 2 inches, whilst the desert tract is almost rainless. This area includes Sind, part of the Punjab and of Rajputana. A zone, with an annual fall of between 15 and 30 inches, borders the arid region on the north and east; a belt of 100 to 200 miles wide. The upper parts of the valley of the Ganges, Central India, and the eastern coast of the Madras Presidency, have a fall of between 30 and 60 inches. A southern dry zone extends from Nasik to Cape Comorin. The deltas of the Mahanadi and Ganges, and the lower part of the Gangetic valley, have a fall of between 60 and 75 inches. There are two belts of excessive rainfall,—one extending along the Arakan coast, from the mouth of the Irawadi up to the valley of the Brahmaputra, the other on the west coast. In these regions the most remarkable falls occur, because they are placed in the direct course of the south-west monsoon, and catch its impact at heights where vapour is most readily condensed into rain. Cherra Punji, in the Khási Hills, where, at 4588 feet above the sea, 600 inches of rain fall in half the year, is on the edge of an abrupt mountain ridge and plateau, situated about 200 miles from the Bay of Bengal; the intervening country being covered with rivers and swamps, over which blows the monsoon, laden with moisture from the ocean. On this plateau the first condensation takes place, and the fall is so great that in a few weeks the plains of the Sylhet district, lying at the foot of the hills, are converted into a sea; while a few miles farther inland, and at little greater elevation, the fall is reduced to less than one-half.

At Mahableshwar, in the Western Ghâts, the conditions are somewhat similar, but there the fall amounts only to about 300 inches.

A general idea of **the climatic conditions of heat and humidity** may be derived from the following table, representing stations throughout India:—

Station.	Elevation.	Yearly Mean Temp.	Mean Max. Temp. of Hottest Month.	Mean Min. Temp. of Coldest Month.	Rainfall.
	Feet.	°	°	°	Inches.
Calcutta[1]	21	78	96	55	65·6
Dacca	22	78	93	55	73·7
Darjiling	7421	51	67	33	127·1
Bombay	37	80	90	68	74·4
Puna	1849	78	101	54	28·3
Belgaum	2550	74	97	58	48·8
Karachi	49	77	93	54	7·8
Jacobabad	186	78	111	43	4·4
Madras	22	82	99	68	49·1
Trichinopoli	275	82	102	67	37·1
Cochin	11	80	91	71	115·1
Bellary	1455	80	104	61	17·6
Utakamand	7252	55	72	35	45·8
Peshawar	1110	70	105	38	13·5
Lahore	732	75	107	43	21·9
Multan	420	76	107	43	7·2
Delhi	718	77	105	48	27·6
Agra	555	79	106	74	26·2
Simla	7048	55	79	36	70·1
Marri	6344	56	83	34	56·6
Mt. Abu	3945	68	89	52	63·1
Ajmere	1611	74	103	44	22·5
Meerut	737	76	102	44	28·5
Allahabad	307	78	106	47	37·6
Nagpur	1025	79	108	54	44·9
Jabalpur	1341	75	104	46	53·6
Indore	1823	74	102	49	36·1
Lucknow	369	78	104	45	37·6
Rangoon	41	79	98	64	99
Akyab	20	79	92	59	195·7
Sibságar	333	73	91	49	93·1
Bangalore	2981	73	93	56	35·6
Trincomalee	175	82	94	74	61·8
Kandy	1696	76	87	68	84·5
Colombo	40	81	88	72	87·3
Newara Eliya	6240	59	71	45	98·9

An important element in climate and health is *irrigation*, by which millions of acres of land otherwise sterile are fertilised; the atmospheric conditions are also modified. There are extensive regions where the normal rainfall is insufficient for agriculture, and without the aid of artificial irrigation the land would be sterile. This is remedied by reservoirs, canals and wells. Where the rainfall is less than 15 inches irrigation is always necessary; where between 30 inches and 60 inches it is often needed, and great distress has been caused by the want of it; where between 60 inches and 75 inches it is looked upon as a luxury, save in exceptional years. Where the rainfall is excessive embankments are necessary to preserve the crops and villages from destructive floods, and the cultivation of land is dependent on their efficiency. Irrigation is now provided to a great extent, and a vast area of land is brought under cultivation. The works, consisting of canals of various sizes, connected with rivers, dams or anicuts, lakes and tanks, are very extensive throughout India: the great rivers, with many other lesser streams, have been laid under contribution for the formation of artificial lakes and reservoirs, and others are in project. Obviously all this must have considerable effect not only on the climate, but also upon the general health of the people; especially as regards fever.

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[1] These particulars are taken from *Climates and Weather of India, Burmah, and Ceylon.* H. F. Blanford.

Another point worthy of notice is the influence of *forests* upon the climate. There is reason to believe that at one time, when the heat of the climate was less extreme, some of the desert plains of India were covered with trees. When we recall the fact that certain desert regions were at one period the seat of early Hindu civilisation and population, it is evident that the physical conditions of the country must have been very different from what they are now; and it seems probable that the change is due to some extent to destruction of trees. The cultivation of forests, therefore, is a matter of great importance, for they temper the climate by the moisture they exhale, and tend to increase the rainfall in comparatively arid regions.

The distribution of moisture is most important as regards climate and health, especially that of the *subsoil water*, its proximity to the surface, and its conditions of movement or of stagnation. The prevalence and intensity of fevers in India are largely influenced by stagnant subsoil water.

The population of India, according to the census of 1891, is over 289 millions, males exceeding females by about one-fiftieth. Of these, 207,731,727 are Hindus, 57,321,164 Muhammadans, 81,044 Eurasians, 100,551 British—the balance being composed of other Asiatics and Europeans, and a few Americans, Africans, and Australians.[1] This large population, averaging generally 184 to the square mile, is of a very mixed character, and comprises members of several of the racial stocks of the world.

To trace the history of these races is not possible within the limits of this article; but as regards their distribution, broadly speaking, Mongoloids predominate in the Himalayas and Burma, Aryans in the Indo-Gangetic plain, and Dravidians and a mixture of Aryans, Mongoloids, and Dravidians in the Deccan. The Muhammadans of mixed races are found more or less all over the country, though less numerous in the south than other parts. Europeans and Eurasians are everywhere. These diversities of race naturally entail diversity of physical and moral attributes; a Russian does not differ more from a Spaniard than does a Sikh from a Bengali, or a Rajput from a peasant of Southern India. Differences of climate, locality and food, combined with racial differences, produce in the inhabitants of India varying capacities for enduring or resisting disease.

As regards **food and habits**, the Hindus, especially the higher castes, subsist chiefly on farinaceous food — wheat in certain regions, rice in others — milk, ghee, vegetables, and fish, with occasionally the flesh of goat or pigeon; the Muhammadans eat a mixed diet. As a rule the natives abstain from alcohol; but Sikhs, low-caste Hindus, and the aborigines drink it freely. Tobacco, hemp, betel and opium—the latter especially in malarial districts—are very generally used. For the most part the natives are abstemious, and the nature of their diet renders them more prone than Europeans to adynamic forms of disease.

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[1] These statistics are from the *Report of the Census of India*, 1891.

Their clothing is generally cotton, or wool in the colder seasons; their habitation simple, generally a hut, often on the ground and ill-ventilated; a mode of living which renders them susceptible to disease.

The social habits of a large proportion of the native population, involving early marriages and frequently sexual excess, tend to lower the vital force, and thus to diminish their powers of resistance to the evil influences of famine to which they are occasionally, and malaria to which they are nearly always exposed.

Europeans and Eurasians may have a tendency to eat more animal food and drink more alcohol than is absolutely necessary, but this has probably diminished of late years. The dwellings of the civil and military population are for the most part good, and the food and occupations, especially of the latter, are carefully regulated. Most Europeans who go to India are selected lives, so that the influence of climate and tropical diseases may be clearly traced in them.

Among such varied climates, races and social customs, not only are the conditions of life widely different, but disease itself assumes various forms and modifications. How far the influences cited operate in regard to the fevers of India is the subject of this article.

SECTION II.—FEVERS

Seasonal Prevalence and Etiology; Distribution. — The official sanitary report for India for 1892 shows that, in that year, **the deaths among the general population under registration** (217,255,655) from all causes were 6,980,785, and of these 4,621,583 were caused by fevers. Registration as regards the general population, though improved of late years, is not yet so perfect as to distinguish the forms, but probably two-thirds might rightly be assigned to malarial, enteric and simple continued fevers.

From three sources, however, more trustworthy information can be obtained; these are the records of—

The European Army, numbering in 1892 (average strength)	68,137
,, Native ,, ,, . . .	127,355
,, Jail population ,, . . .	103,159

In them fevers are registered under the headings "Intermittent, Remittent, Enteric, Simple Continued, and others"; some vagueness probably attaches to the assignments of the three last groups.

In the *British Army* in 1892 the highest mortality from fevers occurred in the months of May and November, the lowest in March and February; in the *Native Army* the highest occurred in January and December, the lowest in April and February; in the *Jail Population* the highest was in April and October, the lowest in January, February, and August. In the *General Population* the highest mortality from fevers occurs in October and November, the lowest in June and July, and the death-rate is nearly twice as great as from all other causes combined. In the British Army the death-rate from fevers greatly exceeds that from any other kind of disease.

In the Jail population cholera, dysentery and diarrhœa caused about five times as many deaths as fevers; whereas in the general population they caused less than one-fourth the number ascribed to fevers. In the British Army these three diseases caused rather less than half as many deaths as did fevers, but in the Native Army they caused one-third more deaths than fevers. From this it may be inferred that the Jail population, however obnoxious to bowel complaints or other diseases, has some immunity from the fever causes which affect other classes not subject to the same vital conditions and restraints.

It is also to be noted that the annual mortality from fever varies less than that from bowel complaints (and especially cholera), which is subject to many fluctuations, depending on seasonal influences and epidemic activity.

TABLE I.—Death-rates from all Causes and Prevalence of Fever Deaths among the General Population in 1892.

Population under registration	217,255,655
Deaths from Fevers	4,621,583
,, ,, Cholera	727,493
,, ,, Dysentery and Diarrhœa . . .	234,370
,, ,, Small-pox	101,121
,, ,, Injuries	85,950
,, ,, all other causes	1,210,268
Deaths from all causes	6,980,785

Seasonal Distribution of Fever Deaths.

Jan.	402,005	July	283,086
Feb.	354,715	Aug.	325,855
March	442,482	Sept.	383,486
April	388,721	Oct.	497,429
May	363,769	Nov.	489,011
June	288,574	Dec.	402,450

TABLE II.—Death-rates from all Causes in the European and Native Armies and Jail Population in 1892.

	European Army, 68,137.		Native Army, 127,355.		Jail Population, 103,159.	
	Total Deaths.	Deaths per mille.	Total Deaths.	Deaths per mille.	Total Deaths.	Deaths per mille.
Fevers	474	6·95	330	2·59	288	2·81
Cholera	121	1·78	272	2·14	488	4·73
Heat-stroke	61	·90	18	·14	41	·40
Dysentery	43	·63	122	·96	805	7·80
Diarrhœa	6	·09	59	·46	203	1·97
Hepatic abscess	75	1·10	11	·09	13	·13
Hepatic congestion and inflammation	6	·09	15	·12	8	·08
All other causes	377	5·53	1079	8·47	1953	18·92
Total	1163	17·07	1906	14·97	3799	36·84

TABLE III.—Seasonal Prevalence of Fevers in the European Army in 1892: 68,137.

Month.	Enteric.		Intermittent.		Remittent.		Simple contd.		Others.		Total.	
	Admis	Deaths.	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.
January	72	26	1,166	1	22	1	123	..	4	..	1,387	28
February	55	14	879	..	23	..	150	..	3	..	1,110	14
March	91	21	1,199	1	27	1	291	..	4	..	1,612	23
April	150	29	1,294	..	54	1	391	..	4	..	1,893	30
May	194	65	1,608	1	85	1	451	..	30	..	2,368	67
June	99	25	1,674	2	54	3	351	1	4	..	2,182	31
July	143	25	1,879	2	95	1	468	.	1	..	2,586	28
August	201	50	2,687	2	95	1	515	1	..	..	3,498	54
September	164	41	3,652	1	105	11	536	..	8	1	4,465	54
October	118	27	5,348	4	106	6	449	1	2	..	6,023	38
November	126	36	5,310	2	166	34	342	..	21	..	5 965	72
December	96	17	2,541	3	62	15	150	..	4	..	2,853	35
Total	1509	376	29,237	19	894	75	4217	3	85	1	35,942	474

TABLE IV.—Seasonal Prevalence of Fevers in the Native Army in 1892: 127,355.

Month.	Enteric.		Intermittent.		Remittent.		Simple contd.		Others.		Total.	
	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.
January	1	1	4,397	12	115	23	51	..	29	..	4,593	36
February	1	1	3,044	9	81	10	49	..	50	1	3,225	21
March	1	..	3 196	10	98	11	92	2	154	..	3,541	23
April	5	..	2,791	4	110	8	130	..	167	..	3,203	12
May	3	3	4,211	9	159	17	285	..	138	1	4,796	30
June	7	3	2,747	13	122	18	133	..	45	..	3,054	34
July	6	2	3,723	6	137	14	170	1	28	..	4,064	23
August	8	..	7,175	14	187	16	156	..	12	..	7,538	30
September	7	2	9,428	6	204	11	95	..	4	..	9,738	19
October	6	2	11,971	10	156	16	118	2	15	..	12,266	30
November	5	..	10,479	19	198	24	82	1	29	..	10,793	44
December	4	2	3,827	13	109	13	40	..	10	..	3,990	28
Total.	54	16	66,989	125	1676	181	1401	6	681	2	70,801	330

TABLE V.—Seasonal Prevalence of Fevers in the Jail Population in 1892: 103,159.

Months.	Enteric.		Intermittent.		Remittent.		Simple contd.		Others.		Total.	
	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.	Admis.	Deaths.
January .	1	..	3,149	5	86	13	274	..	308	..	3,908	18
February .	.	..	2,461	4	66	5	227	..	274	..	3,028	9
March . .	4	1	3,200	8	88	8	298	..	175	2	3,825	19
April . .	1	2	2,840	8	106	20	214	..	73	2	3,234	32
May . .	3	1	3,414	4	71	18	225	..	31	4	3,744	27
June . .	1	..	3,425	3	94	18	113	..	21	1	3,654	22
July . .	5	3	3,237	6	124	13	155	..	8	..	3,526	22
August .	1	1	4,549	1	105	13	226	..	12	3	4,893	18
September .	4	1	7,219	15	167	14	116	..	5	1	7,511	31
October .	2	3	8.074	8	171	23	92	1	18	1	8,357	36
November .	2	..	5,589	12	133	18	111	..	15	1	5,850	31
December .	3	3	3,709	6	85	12	89	1	53	1	3,939	23
Total .	27	15	50,926	80	1293	175	2140	2	1083	16	55,469	288

TABLE VI.—Deaths in the European and Native Armies and Jail Population from Dengue, Typhus, Relapsing Fever, Cerebro-spinal Fever, and other Fevers in 1892:—

	European Army.								Native Army.		Jail Population.	
	Of Bengal.		Of Madras.		Of Bombay.		Of India.					
	Strength, 42,220.		Strength, 13,214.		Strength, 12,703.		Strength, 68,137.		Strength, 127,355.		Strength, 103,159.	
	Admis.	Died.	Admis.	Died.	Admis.	Died.	Admis.	Died.	Admis.	Died.	Admis.	Died.
Dengue . .	21	...	...	...	...	...	21	...	...	...	...	...
Typhus . .	...	...	...	...	...	...	...	...	...	...	...	...
Relapsing fever	...	...	...	...	...	1	...	...	...	...	2	1
Cerebro-spinal fever	...	...	...	...	...	...	...	..	...	...	17	15
Other fevers .	52	1	8	...	4	...	64	1	681	2	1064	...
Total	73	1	8	...	4	1	85	1	681	2	1083	16

The last forty years have seen great improvement in the hygienic conditions of India generally; and, under the auspices of the Sanitary Department, further amelioration may be expected. Practical sanitary work and more enlightened intelligence on the part of the people will, it is to be hoped, gradually enhance their material and moral well-being, and diminish the causes of the fevers still so destructive to them.

As to **seasonal prevalence,** it may be noted that in the hot months, from March till June, fevers of a continued and ardent type occur which are apt to prove dangerous, and seem to be pathologically linked with insolation. They are due chiefly to overheating, but are liable to be modified by malarial influence. In the rainy season, and up to September or October, forms of intermittent, remittent and continued types occur, while there is also a tendency to dysentery and bowel complications. After the rains, during the evaporation and drying up of the ground, fevers of the malarial type become more prevalent.

A high fever mortality seems generally to be associated with an unusually heavy rainfall, and also with defective drainage and water-supply. Of the sanitary importance of a pure water-supply there can be no doubt; it is as essential to preservation from fever as from other diseases, whilst subsoil as well as surface drainage is unquestionably a great preventive remedy. When the cold season sets in, fevers are apt to recur, especially in the early part of it before the system becomes habituated to the change; the weak and anæmic especially suffer, as Twining and others have shown. That such seasonal changes revive fever is well known to old Indians, who frequently find that cold brings on a return of it even after a lapse of years: fatigue and chill are recognised as the most frequent causes of the recurrence of malarial fever at home as well as in India, so that some authorities have ascribed it to chill alone, or even to an excessive amount of water in the blood (hydræmia). It is necessary to make a few general remarks on etiology as it applies to India, before describing the fevers themselves; these will relate chiefly to malarial and enteric fevers.

Etiology.—Before the time of Hippocrates inhabitants of marshy districts were known to be liable to intermittent fever. But it was not until the end of the seventeenth century that Lancisi pointed out its connection with paludal miasmata. The term "malaria" is preferable to paludism, as paroxysmal fevers are not always due to marsh exhalations, being met with also on sandy or rocky soils. Still, the presence of organic matter, moisture, and a temperature above 60°, would seem to be generally requisite.

Whatever its cause, *malaria* is very prevalent throughout India. It was formerly held to be of an aeriform or gaseous nature, though since the time of Varro (114 B.C.), Lucretius (95 B.C.), Columella (50 A.D.), up to Kircher (1602), and Linnæus (1778), it had been surmised that some low form of organism was concerned in its production. In 1866 Salisbury, in America (52), thought he had discovered it in a palmella associated with cells and sporules, to which he gave the name of ague plants. Mitchell of Philadelphia, in 1859, endeavoured to show a cryptogamic origin of malaria. Balestra suspected a species of alga which he discovered in the Pontine marshes. Niemeyer also ascribed malaria to low organisms. Klebs, Tommasi-Crudeli, and others in 1879 described germs or sporules in the soil, water, and air of the Roman Campagna and marshes, which, under a temperature above 20° C. and moisture, rapidly develop into sporigerous bacilli; they did not find them in soil taken from healthy places in Lombardy. It is stated that the bacilli or spores have been found in the marrow of bones, the spleen and blood of persons dying of pernicious fever. During the hot weather the air in malarial districts was said to be charged with bacilli. Stagnant water, however, according to these writers, did not usually appear to contain them.

Lanzi, Terrigi, Marchiafava (35), Cuboni, and French observers in

Algeria assert that they have been able to communicate malarial fever to dogs and rabbits by inoculating them with blood taken from malarial patients. As, however, the *bacteriology of malarial infection* is described in another section of this book, it is not necessary to enter into it further here than to say it is now generally admitted that micro-organisms play a fundamental part in its causation, and that in all cases of malarial fever or cachexia they are not only present, but are the immediate cause. Though it may not be absolutely demonstrated that these are more than epiphenomena, as some have thought, and perhaps still think, notwithstanding the researches of M. Laveran and others; yet it must be admitted that there are strong grounds for accepting this view, albeit the mode of access to the body by the parasite is not yet determined.[1]

It is not the place here to dwell on the part played by micro-organisms in the pathogenesis of malarial fever; even if the disease would not occur without their intervention, yet not less important for its evolution are the predisposing causes and external conditions with which it is associated, and by which its occurrence is determined. These *predisposing causes* exist very generally in India, in certain regions and seasons more intensely than in others. It has been shown that the air of marshes contains a variety of products foreign to the normal atmosphere; for example, excess of carbonic acid, sulphuretted, phosphoretted and free hydrogen, watery vapour, ammonia, organic matter, and the microscopical débris of vegetable and animal matter. The causation of fever seems to be greatly influenced by local and climatic conditions: absent in the arctic, feeble in the temperate, malaria becomes most intense in tropical regions. Water on the surface or in the subsoil, especially when stagnant and near the surface, seems not only to determine the development of the malarious element, but to hold it in suspension. Natives of India attach even less importance to atmospheric states than to water, and firmly believe pools and tanks, or even streams flowing through certain jungles or marshy places, to be charged with fever poison; and many believe that the milk of animals fed in these localities acquires the same property.

There is much evidence to show that when malaria is introduced into the system by drinking-water the effects are more intense and rapid than when it is introduced by air. Testimony is not wanting that in malarial regions those who boil and filter their water have a greater immunity from fever than those who drink it without boiling. Hippocrates and Rhazes both asserted that marsh water caused enlarged spleen and also generated fever, and from that time to the present day such has been the popular belief.

Malaria in India as elsewhere is most active near the surface of the ground. Decreasing in energy it disappears above certain altitudes, given at from 1500 to 7000 feet. How high it permeates the air is not known, but the top of a hill, even the upper room of a house, is less dangerous than the surface or ground floor. Some hill stations of India are not exempt, but, as there is constant communication with the plains and valleys, this may be the result of importation. When people suffer from malaria at elevations above 2000 feet, it may either be derived from unsuspected local sources or carried up by the warm air rising from the plains. It moves like mist up the hillsides, and may be dissipated by or travel with the wind, though no particular limit can be defined. It travels farther over land than over water, especially salt water which is supposed to absorb and retard it. It is said that ships lying to leeward of a malarial shore have been affected by the off-shore wind, charged with emanations from cargoes of green wood or coals, rotting timber or bilge, steeping hemp, jute, indigo, or other vegetable matter; that villages and camps have been affected when to leeward of swamps, even at a considerable distance; that fires, smoke, or a belt of trees will arrest its progress, and that it clings about trees—hence the danger of sleeping under them; it is said also that their growth will destroy or prevent it, and that some, for example the eucalyptus, have a special antagonistic power. This power may be in a great measure due to the rapid growth of these trees, which not only absorbs the moisture from the soil, but quickly creates a protecting screen. It is believed that a muslin mosquito curtain will in some way intercept malaria as well as insects, and that it is not generated where the diurnal range is below 60°. A very high temperature does not always cause, and may even appear to prevent it.

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[1] "Il y a des hypotheses qui jouissent longtemps d'une certaine faveur et que de nouvelles recherches obligent d'abandonner. Tant que dure leur credit provisoire, bon nombre d'esprits trop prompts à conclure les confondent avec les dires absolus de la science, et pendant ce temps-là on se demande comment les mettre d'accord avec l'enseignment" (pathologique).—Monseigneur d'Hulst, quoted in *Witnesses to the Unseen and other Essays*, by Wilfred Ward, p. 78.

Malaria is more active at night than in the day, and more likely to affect those who are exposed to it during sleep, especially if lying on or near the ground. It affects the weak sooner than the strong; the phlegmatic, lymphatic or melancholic rather than the sanguine or nervous temperament; the sickly and ill-fed rather than the robust; the death-rate from fever rising considerably in famine seasons or when there is a scarcity of food. It spares no age; new-comers are more liable to suffer than those who have been acclimatised; yet previous attacks afford no immunity, rather the reverse. It affects all races, but it is reported that negroes acquire a tolerance which has been ascribed without sufficient reason to the colour of the skin. There are certain tribes in the Tarai and other forest districts of India who acquire some immunity. The Tharoos, who inhabit the Tarai, live where it would be death to others, but even they are not altogether exempt.

Malaria is intense in the Tarai and on water-logged land, such as the extensive district of Burdwan, where the free drainage is interrupted by embankments; especially also in districts under artificial irrigation, near rice and other cultivation in some stages, though the danger from fresh rice cultivation is probably exaggerated; and in such localities as the Sundarbans of Bengal, where the alluvial mud is covered with dense jungle and frequently washed by the salt water; also along the sea-coast, where salt and fresh water mingle, and where organic matters decompose in moisture and heat. It is often active, too, on arid, sandy ground, as in the Deccan, Sind, Bikanér, Peshawar, the Punjab, Bhawalpore; but even in these localities subsoil water, damp, and organic matter may be factors; or, it may be, underground water which has percolated from malarial localities: yet it must be admitted that in some of these places the subsoil water lies at a great depth. For example, there are regions in the north-west and in the Punjab which are productive of fever, though their soils are very dry, and are characterised by absence of organic matter. In some of these exceptionally dry soils, which would not be called malarial in the ordinary sense of the term, water is only met with at from 60 to 100 feet below the surface; the soil is practically desiccated. Here one can hardly consider the soil or the air at fault. Whence, then, comes the specific poison, except from the drinking-water, and where does this become contaminated?

In Assam the conditions are exactly the reverse. The land is marshy, and the subsoil water lies near the surface, sometimes with beds of stiff clay close below it, covered with rank, luxuriant vegetation which annually springs up and dies away, leaving the soil laden with organic matter. Here the conditions conventionally considered to be productive of malaria are all present; now both this soil and the dry soil before described produce malarial fever.

It often appears with great virulence after excavation or turning up of soil, and in land that has recently been denuded of jungle. It is interesting to note that in such cases the noxious effects are not always confined to the production of fever. In a remarkable example which occurred in my own experience, a detachment of English soldiers, encamped on some ground in Burma which had been recently denuded of jungle, were attacked by a peculiarly fatal form of dysentery in which the colon rapidly became gangrenous, and by remittent and typho-malarial fever of a very severe and fatal character, as well as by fever in a less severe form. On the other hand, draining and cropping seem after a time to diminish or destroy the poison.

There are regions, formerly populous but now deserted, such as ancient cities the ruins of which are hardly to be traced in dense jungle, which have become notorious sites of fever: there are also places now comparatively healthy that were formerly dangerous. Malaria is at its worst during the drying-up season, after the rains, and at the beginning of the cold season. In the dry, hot weather and during heavy rains, when the ground is covered with water, or when the land has been for some time cultivated and populated (compare Calcutta of to-day with that of a hundred years ago), or covered with trees or even fresh turf, it is less virulent. Certain characters of the soil seem to favour its production. Sandy, porous ground with a substratum of clay, soil containing organic matter, mixed alluvial deposits, volcanic, rocky, granitic soils or surfaces have been thought to favour it. Maclean calls attention to the fact that, when excavations were made in the island of

Hong-Kong, which consists entirely of weathered and decaying granite, and is liable to be permeated with a peculiar fungus, violent and fatal remittent fever appeared. On the other hand, all the conditions supposed to cause malaria may be present, and yet the disease be absent. The low-lying, swampy ground of the Concan and the dry, arid, sandy plains of Marwar are very different, yet malarial fever prevails on both.

Pringle and others thought salt marshes insalubrious; but if, says Moore, salt marshes are deleterious, the neighbourhood of the Sambhar Lake should be deadly; if marshes overflowed by the sea are injurious, the neighbourhood of the Runn of Kutch should be an example: but the fevers in these localities are not worse than those in other parts of the country. Some have even thought that saltness and alkalinity in the soil confer immunity.

It must be admitted that no part of India is exempt from malaria, though its intensity varies greatly. The fevers it produces, more or less intense in different places according to circumstances, may be said to be endemic everywhere throughout it. Not unfrequently, under certain meteorological conditions and failure of food-supply, they assume a dominant and destructive epidemic character, and influence masses of the population far and wide. Some hill stations may practically be exempt; but in the Sub-Himalayan, Indo-Gangetic and peninsular regions, from the desert of Sind to the swamps of Assam, it is universal. It may here be noted that the geographical distribution of malaria is said by Lombard to be within the 65th parallel of north and the 25th or 30th of south latitude. It may be asked, Is malaria always the same, and does it only differ in concentration and activity according to circumstances of season and place? Is that agent which causes severe remittent, simple ague, cachexia and neuralgia, one and the same; or are there different kinds? Is the malaria of the humid Tarai, of the swamps of Assam, or of the Sundarbans, the same as that of the arid sands of Sind? The frequent recurrence of similar conditions in these localities suggests the probability that the poison is one modified by circumstances. Drying-up marshes will most probably cause simple ague, though it is possible that the disease from the same marsh may be more intense under different atmospheric conditions; in this way what are called unhealthy years in the same district may be explained. In all such cases not only the specific and predisposing causes, but the constitution and stamina of the population exposed to its action, have to be considered. The malaria of the Tarai or Sundarbans, and even of the sandy desert, causes dangerous remittent; that of the plains or marshes ordinary ague or milder remittent or cachexia; that of colder regions a variety of indefinite complaints rather suggestive of general ill-health than any specific disease: still, wherever malaria exists the worst forms with pernicious complications may occur. M'Culloch attributed half the ailments in England to local developments of malaria.

Contrary to what might be expected, natives suffer as much if not more than Europeans; no doubt on account of the comparatively unfavourable conditions under which they live. The Europeans are for the most part well housed and fed, and guarded against impure water and other insanitary influences. The natives are more exposed to these, poorly fed, and badly housed. Fifty years ago Europeans died at the rate of 13 per 1000; in ordinary years now less than 7 per 1000 die of this cause. Among the native population the death-rate from fevers is still high, being over 18 per 1000.

Whatever share is to be ascribed to the micro-organism, it would seem to be able to live, or at any rate its pathogenetic action can only be efficient, when in association with other factors which have been hitherto summarised in the vague term malaria or paludism.

SECTION III.—SIMPLE AND MALARIAL FEVERS

It has been remarked that fevers cause a mortality in India greater than that of all other diseases put together; this statement, however, needs qualification, inasmuch as some deaths under this heading would be ascribed to other diseases with febrile characters, were more precise distinctions possible in the registration of deaths among the general population. Still malarial fevers are of universal prevalence, and are answerable for a large amount of suffering and death. It is proposed to deal with these; but, as closely related to them, simple continued, thermic, and enteric fevers will also be considered. Typhus, relapsing, cerebro-spinal, eruptive fevers, and dengue are discussed in other articles of this work.

The fevers to be described may be fairly called climatic, for their incidence, prevalence, and activity—whatever causal part micro-organisms or miasmata may play—are mainly determined by climatic causes. The effects of heat, cold, moisture, and other telluric and meteorological conditions, producing various changes in function and structure, may themselves be efficient causes of fever; may induce autogenetic ptomaine poisoning; may render the body a congenial subject for the development of micro-organisms which act as causes, either directly or by the toxic effects they produce, or may favour the action of telluric miasmata.

Though it is usual to class these fevers under certain well-defined headings, it seems probable that they are nearly allied to each other etiologically, and that a combination of the aforesaid causes, acting on individuals of certain age, race and personal susceptibility, and under the influence of insanitary surroundings, may determine the types assumed. In typical examples the characters may be distinct enough, but it is often hard to discriminate the several fevers. Even periodicity, which is so characteristic a feature of malarial action, is not an absolute criterion; for febrile diseases generally have more or less definite or regular periods of diminution and exacerbation, whilst the plasmodia themselves have not been invariably found in cases of malarial fever.

The diminution of mortality since the introduction of sanitary measures into India shows how amenable fevers are to hygienic remedies. As before stated, the death-rate has been greatly reduced, but it continues higher among the native population because they have not the same sanitary advantages as the Europeans.

Fevers in India differ, indeed, from those in other countries more in degree than in essential nature; the differences being determined chiefly by climate and surroundings. The writings of Pringle (46), Fergusson (19), M'Culloch (37), and others show that there is no fever now prevalent in India which has not at one time or other had its counterpart in Europe, nay, even in our own islands. Enteric fever occurs in India as it does in Europe, and most probably has always existed there, though only of late years brought into prominent notice; it may have been confounded with continued or remittent malarial fever, but it is not by any means certain that a febrile condition accompanied by diarrhœa, Peyerian ulceration, and an abdominal eruption, is necessarily caused by the one specific contagium only to which it is attributed in Europe; for certain forms which clinically and pathologically resemble the typhoid occur in India, and seem to depend more or less on the causes that give rise to malarial diseases. Admitting, then, that the enteric fever of Europe is found in India, it may still be questioned whether similar phenomena may not occur during the course of certain forms of malarial fever. The frequency of cases so terminating, which have begun with characteristic malarial symptoms, and have not been exposed to causes which give rise to enteric fever in Europe, seem to render this probable.

Ephemeral Fever, Febricula, or Simple Continued Fever.—A simple form of fever is common in India, and is most frequent in the hot and rainy season, from which all may suffer; new-comers are, however, specially liable to it. It appears to depend rather on the new and altered conditions of life under which the patient finds himself placed, than on any specific miasm or micro-organism. Heat, alternations of temperature and chills, excess or errors in food or drink, anxiety, the restlessness and want of sleep due to heat, the irritation of mosquitoes and other insects, derangement of digestive functions, disturbed innervation and metabolism, blood contamination from retention of effete products the result of imperfect assimilation and elimination, cause a state of febrile disturbance which may be regarded as an acclimatising process—a readjustment of the organism to its new surroundings.

This form of fever is sudden in its onset, and in ordinary and favourable cases rapid in defervescence. In twenty-four to seventy-two hours we may see the patient restored to health, though the fever is often prolonged over several days; this, however, is infrequent unless there be complications or relapse.

The symptoms are lassitude, malaise, muscular pain, headache, coated white tongue, nausea or even vomiting, chills, a speedy accession of high temperature (102° or 104° F.), the maximum only lasting a few hours, and soon followed by sweating. The urine during the paroxysm is scanty, acid, of high specific gravity, and contains a large amount of urea and other solids; the quantity of the secretion augments as defervescence takes place. The pulse is full and often firm, with varying degrees of rapidity. After defervescence health is quickly regained.

In plethoric or intemperate persons the reaction may be more severe with high fever and delirium, and visceral complications may occur and increase the urgency.

In natives or old European residents these attacks are likely to be complicated with malarial poison, and modified or intensified thereby; and they may pass on to assume a paroxysmal or even enteric character.

This fever generally yields readily to simple treatment. The patient should be confined to his bed or to his room, which should be kept cool by punkah or thermantidote; the bowels should be freely moved; diaphoretics, consisting of the acetate of ammonia, acetate or salicylate of potash, nitrous ether, and camphor mixture, should be given during pyrexia. If there be much heat or pain in the head ice may be applied, or, in very plethoric persons, a few leeches to the temples; but this is very rarely necessary. The body may be sponged with tepid water; cooling drinks should be given while the thirst, which is often great, continues. All excitement should be interdicted. The diet should be light and simple, chiefly fluid for the first few days. Care should be taken during and for some time after recovery to avoid any errors of diet, excitement, fatigue or chill. There should be complete rest and a cautious return to the usual diet before resuming ordinary occupations.

It may be beneficial for the patient to take three or four grains of quinine twice a day in some bitter infusion for some days after recovery is apparently complete.

Complications—hepatic, pulmonary, or gastro-intestinal—should be dealt with according to the indications.

Thermic or Ardent Fever.—This is a more serious form of continued fever, varying from slight to intense pyrexia. It chiefly occurs in the hot season, when it may result from direct exposure to solar rays or to the highly-heated atmosphere. During the hot winds natives frequently succumb to it. A fatal issue may be immediate or induced less rapidly by hyperpyrexia, the result of vaso-motor paralysis and failure of the respiratory centre. The body temperature may rise to 108° F. or higher.

The ordinary ephemeral fever may pass into this stage; especially when the heated atmosphere is laden with moisture which interferes with evaporation, and thus impedes the natural refrigerating processes of the human body. It is probable that a considerable number of cases recorded as continued fever are of this nature, originating when the heat is intense, the atmosphere impure and humid, the surroundings unhygienic, and the habits irregular or intemperate. They may be, but are not necessarily, complicated with malarial infection. The more serious effects of exposure to great heat, which are frequently fatal, or result in permanent injury to the nerve centres, are described in the article on

Insolation. Some cases resulting from exposure to the sun are very slight and transient in their nature, passing away in a few hours. These may be called sun fever; between them and the most severe forms of ardent or thermic fever there is every gradation of intensity.

In ordinary cases of thermic fever the symptoms are similar to those of ephemeral or simple intermittent fever,—malaise, muscular pain, headache, nausea or vomiting, chills rapidly followed by pungent heat of skin, flushing of the face, and it may be delirium, with a rapid rise of temperature to 104° or 105° F., or even higher: this may continue for some days with slight but varying remissions, and generally terminates with diaphoresis. The urine is scanty or may be suppressed, the perspiration has a peculiar odour. When the temperature rises above 105° or 106° F. the state is one of considerable danger.

In the milder forms this disease yields readily to treatment, and under favourable circumstances recovery quickly takes place. The main object is to reduce the temperature, for which active measures are needed; perfect rest in a cool atmosphere (if it can be secured), free evacuation of the bowels by moderate doses of calomel and by saline purgatives, cold douches, cooling drinks, and ice to the head must be prescribed; care being taken not to depress the patient unduly. Diaphoretics with antipyrin, phenacetin or aconite should be given. Nourishment must be of the lightest kind.

Quinine here may be of service on account of its antipyretic properties, and it may be given either by the mouth, or, if the case be urgent and the high temperature suggest immediate danger, hypodermically. As defervescence takes place and the normal temperature is regained, the greatest care must be taken to prevent relapse; and whilst the often profoundly exhausted condition due to the high fever may call for stimulants and invigorating remedies, errors in diet or in alcoholic stimulants must be sedulously avoided. It will be expedient to continue the administration of quinine or other tonic remedies for some time after recovery, especially if there be any suspicion of a malarial taint; and to observe the greatest caution in permitting resumption of work or duty: whilst especial care must be taken to avoid exposure to the direct heat of the sun or to an overheated atmosphere.

The various complications which may arise when ardent fever passes into insolation, of which it is so frequently the precursor, and the methods of dealing with them, are described in this work in the article on Insolation [vol. i. p. 491].

As a result of my own experience, I am of opinion that although these cases generally do well, and recover after varying degrees of intensity and duration, from some cause or other they may pass into a fever of a low type, and ultimately prove fatal with all the symptoms of the enteric form. Whether this be the result of the continued evolution of the fever process, or whether it may be due to the supervention of a miasmatic or parasitic agent, I am unable to say; though I believe that low remittent forms of fever accompanied by Peyerian ulceration and diarrhœa may be a natural result of the original cause, without the introduction of a specific microbe.

Intermittent Fever or Ague.—Malarial fevers are fully described in the article set apart for them. Fever, however, is not the only expression of malarial action; cachexia not preceded by fever, in which important pathological changes occur, may be produced and continue for years with other protean manifestations. These will be considered in the description of masked malaria fever and cachexia.

Intermittent fever in India resembles that which occurs elsewhere. There are the same premonitory symptoms, the same evidence of disturbed vaso-motor action, congestion, and derangement of abdominal viscera, and to a certain extent a similarity of type. However much other manifestations of malarial fever may vary according to locality, an attack of simple ague is much the same wherever it occurs.

The phenomena of a paroxysm closely resemble those of ephemeral or thermic fever, but they are subject to great modifications. There are sometimes herpetic eruptions on the lips and occasionally urticaria. The stages may vary in intensity or duration, or one or other of them may be absent, or so slightly expressed as to be hardly recognisable. The cold stage may vary from a transient chill to severe convulsive rigors; it may last a few minutes, or it may endure for hours, in which case danger may be imminent. The hot stage may vary from a moderate rise of temperature to hyperpyrexia with intense congestion, headache, and violent delirium; or it may pass into the stage of collapse known as the algid condition. The sweating stage may vary from slight moisture to drenching perspiration attended with great exhaustion. To such modifications the term pernicious may be given.

From the fact that these paroxysms have a tendency to recur at certain intervals, malarial intermittents have been designated as quotidians, which recur in twenty-four hours, tertians in forty-eight, and quartans in seventy-two hours. These have been further divided into double quotidian, double tertian, double quartan, and so on, whilst in some cases the intervals have been extended to weeks, months, and years.

The quotidian may have two paroxysms daily. The paroxysms of tertian fever may recur every day, those on alternate days corresponding; this is called double tertian or *tertiana duplex*. When the intermission is incomplete it is called either a remittent of the double tertian type, or double tertian with subintrant paroxysms. In another form of tertian the paroxysms occur on each alternate day, but twice in the day; this is doubled tertian or *tertiana duplicata*. In quartan the paroxysms may occur daily, those of every fourth day resembling each other; this is triple quartan or *quartana triplex*. In another form of quartan the third day is free from fever, the paroxysms corresponding every fourth day as in the previous type; this is *quartana duplex*. When two or three paroxysms occur every fourth day we have a *quartana duplicata* or *triplicata* as the case may be. Further modifications have been recognised by nosologists as quintan, sextan, octan; but these seem to be refinements of little practical value.

The average duration of the fit is said to be about sixteen hours in the quotidian, ten in the tertian, and six in the quartan; but these are subject to much variation. The period of access is generally early morning for the quotidian, noon for the tertian, three to five for the quartan. These are also very variable, and are liable to confusion where the cases are regarded as double recurrences.

As to the relative frequency of the different types, quotidian is most frequent in India. According to Waring, observations in India and in the Tenasserim provinces showed that of 2574 cases of ague, 1822 were quotidian, 595 tertian, 29 quartan, 118 double tertian, 10 irregular; also that of 53,753 admissions of European soldiers in the Bengal Presidency for intermittent fever, 51,287 were quotidian with 646 deaths, 2097 tertian with 12 deaths, and 369 quartan with 2 deaths. Dr. Burton Brown says that at least 95 per cent of the fever cases at Lahore are quotidian, about 3 per cent tertian, the rest quartan, remittent, or enteric fever.

In Bombay, according to Morehead, of 243 cases in natives, 211 were quotidian, 27 tertian, and of 5 the type was not recorded. Chevers says in Lower Bengal intermittent fever assumes the quotidian type in natives and tertian in Europeans. According to Morehead, quotidian prevails in the south-west monsoon, tertian in the cold season as the result of alternations of temperature, and in those who have resided long in malarial localities. In another table of fevers from different localities of India, Waring gives the following results:—Quotidian 4458 = 79·7 per cent; tertian 900 = 10·1 per cent; quartan 102 = 1·8 per cent; double tertian 119 = 2·1 per cent; irregular 10 = 0·17 per cent. The proportion of quotidian was larger by 16 per cent in the Bengal than in the Madras returns, while the tertian was about 15 per cent less.

Quotidian is no doubt the most frequent form, but in my experience the day and hour of recurrence are apt to be most irregular; and were it not that the definite types are more distinctly marked in other parts of the world, designations denoting a certain fixed period would scarcely have been adopted in India. This irregularity may be peculiar to Indian paroxysmal fevers, and perhaps to those of other hot or tropical climates; in temperate climates the periods may be more regular; but my experience of Indian fevers in England affords evidence of irregularity even greater than in India.

I have often seen cases like the following:—A young officer, invalided for a severe malarial fever, is exempt from recurrence during the greater part of the passage home. He lands in England, very weak and exhausted by former illness, but still quite free from fever for many days. He is very much fatigued by the exertion of landing, gets wet through by rain, and is chilled. He arrives in London still fairly well and eats a good dinner, but has a restless night, much malaise, and discomfort. The following morning he is attacked with rigors which last for some hours, followed by a hot stage in which the thermometer rises to above 106°, and then passes into a state of profuse perspiration and exhaustion of an alarming character. Five-grain doses of quinine are administered every three hours, stimulants and nourishment are given. For two or three days after this he improves, the thermometer falling to a degree below the normal. He gradually regains strength, and in a day or two is able to proceed on his journey, no recurrence of the fever having taken place. He is warned that chill, fatigue or errors in diet will almost certainly reproduce another paroxysm, and that in any case, however careful he may be, he must expect some recurrences of the fever before perfect restoration to health.

It is probable that the early use of antiperiodic remedies modifies the course and phenomena of the disease, may render the return of the paroxysm irregular, or perhaps transform ague into remittent, or the converse. Determinate periods are probably not of much pathological significance, and when a man contracts malarial fever the type will depend on himself and his surroundings, rather than on a difference in the nature of the cause. The difficulties in accepting the doctrine that assigns each form to a separate micro-organism are great: it seems negatived by the readiness with which a change in the type may occur.

As regards *incubation* various periods have been assigned, from a few days to three weeks or a month; but from the occasional supervention of symptoms almost immediately after exposure to intense forms of malarial poison, there is some reason to believe that its action may be speedy, though the possibility of previous exposure must not be forgotten. Perhaps eight to ten days may be considered the average period of incubation for ordinary attacks of malarial fever; the intensity of the poison, the susceptibility of the individual, and the character of the locality probably determine the duration of incubation and the form the disease may assume. Where a party of men have been exposed to the emanations of a malarial locality, one will only feel rather ill, another will have ague, another remittent, another dysenteric or even choleraic symptoms.

The appearance of the first paroxysm of ague is not to be taken as determining the duration of the period of incubation; for symptoms of a less definite kind often precede it and at last terminate in the fit. Sometimes no distinct febrile paroxysm occurs at all, but the patient lapses gradually into a state of malarial cachexia.

Remittent Fever.—In India, as in other tropical countries, malarial fever is very apt to assume the so-called remittent form. In simple cases the paroxysmal character is observed, but a complete intermission is not attained; the temperature does not subside to the normal range, the fever merely remits until the return of the paroxysm. The type and character probably depend upon the intensity of the poisoning, the state of the person who is the subject of it, and the character of the prevailing epidemic; for malarial fevers, though generally endemic, do sometimes assume the epidemic form.

A remittent malarial fever is as truly a continued fever as is the enteric or any other of the specific fevers which have fluctuations of temperature during their progress. All the manifestations of malarial disease might be classed under the heads of malarial intermittent, malarial continued fevers, and cachexia, the modifications of the action of the poison being regarded as accidental complications; but it is not possible in the present state of our knowledge to say with certainty what determines the special type. However this may be, the intermittent may become remittent, or the remittent intermittent; and both alike may induce the state known as malarial cachexia.

As already stated, almost any part of India may give rise to simple ague; but such regions as the Sundarbans, the Tarai, debouchures of great rivers, and other localities where dense jungle, uncultivated soil, perennial marshes, water-logged land, a humid atmosphere and high temperature prevail—to which may be added certain localities having an opposite character, such as parts of the desert region—are often productive of remittent, continued and typho-malarial fevers.

The season of the year has a considerable influence; for example, the greatest number of admissions in the European army in 1892 were in October and November, and the greatest number of deaths among the general population in October and November[1] (*vide* Tables I. and III.) But as no part of India, except perhaps some of the higher hill stations, can be said to be exempt from malaria, so at no season can it be said to be totally in abeyance; and fever from the simplest ague to the most intense typho-malarial poisoning may occur in almost any locality or season, though most especially in those indicated.

The result of my experience in India, and subsequently in this country, is that from whatever part of India the subjects come, the identity of the disease and the general similarity of the consequences are unquestionably admitted. Fevers are wont to be designated by such terms as Peshawar, Bengal, Deccan, Sind, Arakan fever, etc. etc.; Tarai, jungle fever, etc.; these are, however, all expressions of malarial poisoning of different intensity and local variation, and they differ in degree rather than in kind.

Symptomatology.—An attack of remittent fever, like ague, may have its premonitory symptoms, which resemble those of intermittent fever. After a few days, or perhaps suddenly, chills or even rigors set in, though perhaps less frequently and severely, the cold stage being generally of much shorter duration or even absent. The temperature then rises and continues to rise to 104°, 106° or 107° F. The hot stage may last for from six or seven hours or less to forty-eight hours or more.

There may be gastro-intestinal irritation, nausea and vomiting; the liver is often involved, as shown by hypochondriac tenderness, which may be due either to the liver or to the congested duodenum; there is occasionally jaundice or an icteric tinge of the skin and bilious vomiting, which, when excessive, characterise the fever as bilious remittent. The tongue is coated, often stained a yellowish tint, and may become dry and brown, the headache is intense, there may be epistaxis, and pain in the eyeballs; delirium is often present, the skin very hot, the pulse hard and quick, the thirst great.[1] These gradually pass away with a sweating stage not so long or pronounced as in intermittent fever; sometimes they are almost imperceptible. The temperature falls, but not to the normal standard, the pulse becomes softer, and the sufferer is relieved, though want of sleep is often a distressing symptom. This remission may last from two or three to thirty or thirty-six hours, when the fever returns. Such recurrences may continue from day to day, ordinary cases lasting for a week, mild cases only for three or four days; and then either there is gradual return to health, or intermittent fever in the quotidian, tertian or irregular form may supervene; or the symptoms may be aggravated till they assume the bilious, the gastric or the typhoid type. In the adynamic conditions which occur so frequently among natives, especially in the cold weather and famine seasons when food is scarce, pneumonia, enteric ulceration, exhaustive diarrhœa with dry, brown tongue, and cerebral and typhoid symptoms, may intensify the danger and increase the mortality.

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[1] The admissions for the general population are not recorded.

Although the accession is generally said to appear at noon or early in the afternoon, yet the recurrence of the paroxysm and the length of each stage is of extreme irregularity, being influenced both by natural causes and by cinchonism. The first exacerbation is often the longest, but the second is frequently more severe, and may set in without any premonitory chills or cold stage. If not now checked, succeeding paroxysms may become more severe with scarcely any remission; and great prostration with delirium and unconsciousness, a dry brown tongue with sordes, yellowness of the skin, high-coloured urine, vomiting of bile and altered blood (so called black vomit), hæmaturia and hiccough may supervene, and often end fatally.

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[1] The following is an interesting example of the severe modifications this form of fever may assume. The Annual Report of the Sanitary Commissioner with the Central Provinces for 1881 contains an interesting account of a supposed new type of fever by Surgeon-Major Evers of Wardha, a district of Nagpore. The climate of Wardha is characterised by sudden and rapid changes of temperature. The average rainfall is 30 in., but in 1881 it was 54 in. —exceptionally heavy. All the physical conditions which favour malaria exist in abundance. Fever in all its forms, from the slightest febrile disturbance to the most fatal stupor, occurs; and the mortality is higher in the district than in the towns. Dr. Evers writes that in the month of September, just after the appearance of cholera, he noticed that violent vomiting and diarrhœa preceded the setting in of many of the cases of remittent fever. These cases, if neglected, soon passed into a typhoid condition; but after the first violent diarrhœa there was obstinate constipation which yielded only to strong saline purgatives. Quinine and stimulants were absolutely necessary in the treatment. Dr. Evers, in the course of his inspections, noted the occurrence of certain cases, and these, under the designation of a new disease, are referred to in the Sanitary Commissioner's Report. They occurred during the winter season in an elevated region in the district of Wardha. The sufferers seem to have been of the aboriginal, that is, non-Aryan section of the population. The symptoms of the disease seem to have been intense headache, high fever which did not remit until bleeding from the nose, stomach, and bowels, and vomiting of bile, occurred; after which the body became cold and jaundiced; unconsciousness, picking of the bed-clothes and death following in a few days. No post-mortems were obtained. It is probable that this was only one of many ways in which heat, miasmatic influences, malaria, and foul water may affect those who are exposed to them in their intense forms. Dr. Evers inclined to the belief that the disease might have been acute yellow atrophy of the liver; the assistant surgeon described such cases as yellow fever. Malarial remittent fever, however, as is well known, sometimes simulates specific yellow fever; when, for example, black vomit and jaundice are present. In the absence of a more detailed account of the symptoms during life, and of any description of the appearances after death, it is difficult to form an opinion as to the precise nature of these cases; but it seems probable that they were manifestations of one of many ways in which the above-mentioned causes all combined, and each in an intense form may operate: and are an illustration of the protean forms which local influences, personal susceptibility, and various other conditions may cause malarial infection to assume.

The character of the remissions and the early or deferred return of the exacerbations indicate the probable severity or lenity of the attack. Well-marked remissions, free diaphoresis, reduction of temperature, diminished headache and cerebral symptoms are favourable indications; whereas accelerated exacerbations, higher temperature, and ill-defined remissions with typhoid symptoms, delirium and coma, vomiting of blood or bile, diarrhœa and collapse, as the hot stage is passing away, are indications of extreme danger.

In favourable cases amendment begins in from three or four to six or eight days. The remissions are well marked, the patient sweats freely, the tongue begins to clean and moisten at the edges, and the sordes to disappear; the headache and thirst diminish, the appetite begins to return, the patient probably sleeps and gradually regains his strength.

Complications.—In simple attacks of remittent fever the prognosis is favourable; but, under certain circumstances, cerebral, pulmonary, hepatic, splenic, gastro-intestinal or renal symptoms may suddenly set in. In the robust and plethoric young Englishman the disease assumes the sthenic form; high fever, a full and strong pulse, intense headache, epistaxis and delirium, are followed by a well-marked remission and much exhaustion. Such cases may be complicated by exposure to great solar heat, or by the previous abuse of alcohol. In weaker persons the tendency is to assume the adynamic form; exacerbations may reduplicate, nerve force be depressed, and fever become continued, or pass into a low, tremulous, typhoid form. Sudden collapse sometimes supervenes, or convulsions may take place, especially in children; inflammatory cerebral mischief may occur, occasionally with coma.

In the thoracic and abdominal viscera complications may arise, and the natives of India in the cold season are peculiarly prone to suffer. The spleen is not always much enlarged at first, nor are the cachexia and anæmia well marked, unless the disease have continued long or recurred often. Albuminuria may occur, but is comparatively rare in remittent fever.

In the *typho-malarial form* diarrhœa sets in, and the evacuations have the pea-soup appearance of those of enteric fever. There is abdominal distension, pain and gurgling in the iliac fossa, indeed the symptoms generally of typhoid; and these may run on to a fatal termination. In such cases it is difficult to distinguish the state from specific enteric fever. The history of the case, its origin and progress are the only valid guides. Such cases may depend on a joint action of malarial infection and the specific poison of enteric, but I have long been of opinion that the fever processes of malaria are sufficient under certain circumstances to give rise to it, though I in no way deny the existence of enteric fever in India independent of malaria.

Pernicious Attacks.—The conditions termed pernicious occur in the intermittent and remittent forms, as intensifications of any of the stages. The cold stage may be unduly prolonged and occupy the whole paroxysm; the patient either sinking in a state of collapse with choleraic symptoms, as occurs in some epidemic outbreaks in India, as at Amritsar in 1881, Peshawar in 1892,[1] and frequently elsewhere; or in other cases assuming a dysenteric aspect; or reaction may take place slowly; or the hot stage may be intensified or prolonged, the patient becoming delirious, comatose, convulsed, with a very high temperature, so that the condition resembles that of thermic fever or insolation: yet in the hot stage the algid condition may rapidly supervene. Stupor begins with the commencement of the paroxysm, and gradually deepens into complete coma or death; or the symptoms may gradually disappear as the period passes away. Again, the sweating stage may be very profuse and prolonged, the pulse may sink, and the depression be so great that death takes place from exhaustion and syncope; or after the sweating stage has passed, increasing depression may continue; the patient is conscious, but hardly sensible of his own weakness or of the danger of any exertion. In this state an attempt to assume the erect posture is dangerous, as it may induce fatal syncope.

The immediate explanation of the supervention of pernicious symptoms is not very clear. They sometimes come on with little warning, after one or two ordinary paroxysms of intermittent fever; at other times in the course of more serious remittent forms, most frequently perhaps, but not always, in subjects who have been much debilitated by the disease. It is during the damp heat of hot months in certain parts of India that these grave symptoms are most likely to occur.

Hæmoglobinuria, indicative of injury to the blood corpuscles, is apt to occur in some forms of malarial fever. This happens much more frequently in Africa and other tropical regions than in India, as shown by Crosse. In this state the urine contains hæmoglobin or pigment derived from it; the contents of the bowels and stomach are discoloured from the same cause. The presence of pigment in any of the organs and tissues is considered to be conclusive of the malarial origin of the disease. When hæmoglobinuria occurs in Indian forms of fever it is of evil augury, though not by any means always fatal; for, with other complications, as the paroxysm passes over it may also disappear. [*Vide* article "Hæmoglobinuric Fever" in a later volume.]

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[1] In Peshawar in 1892 the malarial fever was of a specially severe type, and prevailed mostly during the months of September, October, November, and December. In this period there were fifty-four deaths from remittent fever. In the early cases it was extremely difficult to diagnose them from cholera, the patient being attacked with purging, vomiting, cramps and suppression of urine, quickly followed by collapse. At autopsy, liver and spleen were found greatly congested, the spleen in some cases weighing thirty to forty ounces. The cause of this unusual sickness was generally attributed to the heavy rainfall in July and August.

Other unfavourable symptoms indicating complication of the nerve centres may be attributed to the presence of the micro-organisms, or to emboli in the small vessels depending either upon small clots or pigment infarctions; these cause paralytic, aphasic, or other cerebral symptoms, or blindness: emboli or intravascular clotting occurring in the larger vessels may cause obstructed circulation and even gangrene in the limbs or other parts of the body, such as the lungs, liver, spleen or other abdominal viscera; or when they occur in the right side of the heart they may cause dangerous and even fatal symptoms by plugging the pulmonary artery.

Masked and Irregular Malarial Fever.—The action of malaria is also occasionally expressed by the conditions which are described as masked fever. Malaise, neuralgia in the form of hemicrania or brow ague, in the brachial plexus and in the intercostal nerves, in the branches of the fifth and occipital nerves, in the great sciatic, or indeed in any part of the body, accompanied by imperfectly developed fever, convulsions in children, gastralgia, local anæsthesia and paresis, aching in the limbs, pain extending along the course of the great nerve-trunks, functional derangement of the liver, nervous irritability, dyspepsia, even hæmaturia, bronchial irritability, dyspnœa, and asthma, and a variety of other symptoms, point to the effects of malarial poison on the nervous system, though fever may even be absent.

Other forms of masked fever may be collapse as in cholera, hæmorrhage from the stomach, bowel, bladder or kidney (in which case, probably, some hepatic or other visceral complication may coexist), cerebral effusion, or apoplexy with epileptiform convulsions. The circumstances under which these pernicious conditions arise suggest their nature and origin, a suggestion frequently confirmed by the successful results of their treatment by quinine or other antiperiodic remedies. These phenomena have generally a periodic tendency, and are influenced by atmospheric conditions—the natives of India think by lunar changes. Morehead, Peel and others refer to this, and, speaking of the recurrence of malarial symptoms on days on which they are coincident with lunar changes, note that atmospheric changes were generally observed on these days, and that it was due to the latter.

In neuralgic attacks it is possible that an original tendency to this malady may have been intensified and rendered periodic by the action of malarial poison.

Twining pointed out that the frequency and obstinacy of the visceral diseases which accompany malarial fever in India are characteristic; and there is hardly any organ that is not sometimes found affected either functionally or structurally.

In persons who have been long subject to paroxysmal fevers in which there is a frequent recurrence of the cold stage, the liver, spleen, and portal circulation are apt to be affected, the spleen often very rapidly.

It is after repeated recurrence of these paroxysms that the visceral changes appear which lead to a state of anæmia, cachexia and debility. It may be noticed that the chief causes of the recurrence of irregular forms of fever in this country are sudden changes of temperature with chill, mental and physical fatigue, and errors of diet.

Urethral and Elephantoid Fever.—Attention may here be directed to another morbid tendency of those who are the subject of malarial poisoning, the so-called urethral fever (18*c*), so apt to follow on catheterism, however skilfully performed. The mere passage of an instrument, however easily, will in some cases produce a severe attack of rigors, followed by fever and sweating, in some cases by symptoms of a pyæmic nature, with the formation of abscesses in remote localities, or again an algid, cerebral or typhoid form, which may prove fatal: as a general rule, however, such attacks terminate favourably.

Another form of fever, probably filarial in its origin and connected with elephantiasis, as pointed out by Bancroft, Lewis, myself, and others, and especially by Manson, to whom the discovery of the filaria is due, though complicated by malaria, occasionally occurs, and is called elephantoid. It attends the periodic hyperæmia which frequently leads to permanent hypertrophy. This condition is associated with a disordered and dilated state of the lymphatic vessels. The prostate gland, the spermatic cords, the epididymis, and the scrotum are congested and swollen, the latter often with an acute erythematous inflammatory condition which ends with desquamation. These symptoms are sometimes attended with gastralgia, nausea, great suffering and high fever. Though probably essentially filarial in its origin, it is apparently so closely connected with malaria, that it seems right to mention it here. [*Vide* article on "Filaria" in this volume.]

Inflammation of the parotid glands and orchitis sometimes occur as complications of malarial fever; but the causal relation of malaria to these conditions has not been very clearly established. I pointed out many years ago that hydrocele was frequently due to malaria (18*c*).

Burdel found *sugar in the urine* of eighty out of eighty-six cases of intermittent fever; especially in pregnant or suckling women and in pernicious forms. Verneuil concluded that malaria occasionally engenders glycosuria in one of two forms: one contemporaneous with the attack of fever and transient; the other more tardy in onset, independent of the paroxysms, and permanent. My experience confirms its occasional occurrence. It is possible that the general perturbation and increased blood-pressure of malarial poisoning may be the cause of glycosuria.

Chronic Malarial Infection.—A frequent result of long residence in a malarial climate, and of repeated attacks of periodic fever, are anæmia and cachexia, with which may be associated structural changes in the abdominal viscera, notably in the spleen, and occasionally—of a cirrhotic character—in the liver. In advanced cases the symptoms are puffy, blanched face, pallid lips and conjunctivæ with pearly sclerotic, short and hurried respirations or dyspnœa, occasionally temperature a degree or two below the normal, weak cardiac action sometimes with hæmic murmurs, a feeble pulse, epistaxis, vertigo. The abdomen is tumid and sometimes dropsical; there may be œdema of the lungs and of the areolar tissue, especially of the legs and feet; wasted muscles; a pigmented and pale skin; a large and probably hardened spleen, extending below the ribs to the umbilicus, or even to the iliac fossa (ague cake); vomiting and diarrhœa, which not infrequently assumes the white tropical form; coated tongue; loss of appetite; chronic muscular or rheumatic pains; asthma; neuralgia, and other indications of disturbed innervation and nutrition; hot hands and feet, with occasional rises of temperature and even slight and irregular paroxysms of fever. The blood is altered, the red corpuscles are diminished in number from 4,500,000 to 2,000,000 or 1,000,000 per cubic millimetre (Laveran); the white corpuscles are relatively if not actually increased in numbers; the specific parasites in various stages of development are found, and there is tendency to intravascular coagulation, which may prove dangerous, if not fatal, by plugging the pulmonary artery or any part of the arterial or venous systems, causing in the first case danger or death, and in the second embolism and even gangrene. The least wound or abrasion is liable to bleed profusely or to become gangrenous; the gums are spongy and bleed; the teeth become exposed and finally fall out: gangrene of the scrotum or *cancrum oris* occurs frequently among the natives of India.

The kidneys occasionally suffer; the urine is of low specific gravity, and contains albumin and renal casts. Albuminuria, however, is not frequent, nor is it, when of small quantity, necessarily of such serious importance as might be supposed.

The condition in which some one or more of the foregoing symptoms are present is common enough in the notoriously malarial regions of India, where physical degeneration is accompanied by an almost equally well-marked physical and mental torpor.

Malarial cachexia occurs also without any previous fever, the process being one of failing health and slowly progressive anæmia—indicated by increased debility and incapacity for mental and physical exertion, gradually merging into the condition already described. Occasionally, however, it supervenes rapidly after a few attacks of fever. Europeans generally leave India before matters have advanced to the later stages, though they not infrequently return to their own country too late to profit by the change; they are often surprised by having their first attack of fever after leaving India on account of protracted cachexia.

Cachexia is often of long duration, and the only hope of recovery lies in leaving the malarial district, and, for Europeans, returning to their own country, where, under the influence of change of air and careful treatment, the symptoms are mitigated and gradually disappear; though in advanced cases the condition is a very precarious one owing to the tendency to dangerous complications, whether renal, pulmonary or cardiac. Catrin, in his admirable treatise on *Paludisme Chronique*, says:

"Si l'impaludé chronique reste dans la region où il a contracté son affection, l'aboutissant le plus fréquent, c'est la cachexie avec toutes ses conséquences et son issue fatal." Happily a number of cases are not of this severity; the symptoms are much less marked, the cachexia is not so far advanced, and the malarial taint expresses itself by anæmia, functional derangement of the digestive and assimilative apparatus, a tendency to irregular recurrence of fever, and occasionally sweating without any obvious cause. In some cases there is enlargement of the spleen, in all a sallow and somewhat pigmented skin and a general deterioration of health. Such persons under the influence of change of climate, judicious management and the use of appropriate remedies, are generally restored to health; but they afford evidence of the pertinacity with which the malarial taint clings to those who have acquired it, and the length of time which is needed, even under judicious management and mode of life, to get rid of the vestiges of it. In them the peculiar diathesis imparted by previous malarial infection is shown by the periodic character assumed by other ailments, and by the disposition to recurrence of malarial action, such as slight fever, sweats, neuralgia, dyspepsia, diarrhœa alba, long after the generally sound conditions of health seem to have been established.

The cases of profound splenic cachexia, where the spleen is chronically enlarged, though not hopeless, give rise to the greatest anxiety lest they prove fatal in any of the ways just referred to from the utter inability of the patient to resist any accidental complications or emergencies which may arise.

Pathological Anatomy.—Death in uncomplicated ague is rare; but in the remittent and pernicious forms, and from complications and sequels, it is frequent.

In *acute malarial poisoning*, especially where death occurs early, there may be no evident structural change, except that pigmentation is present in many organs. The *spleen* will often be found somewhat enlarged, the capsule thinned and stretched, and the substance of the organ diffluent and of a dark chocolate colour, due to accumulation of pigmented elements and débris. If the autopsy be made soon after death, parasites in various stages will be found; but they seem soon to disappear.

The *liver* is discoloured by pigment in the small vessels, and sometimes a little enlarged. The *kidneys* in simple cases are normal, but on section pigment is collected, especially in the glomeruli. In the bilious hæmorrhagic form of fever they are increased in size and weight, and under the capsule exudations of blood are found, whilst section reveals the substance of the kidney to contain small interstitial hæmorrhages. The *intestinal tract* is unaffected unless complicated with dysenteric or enteric ulceration. In the *lungs* there may be a certain amount of hepatisation or congestion. The *heart* is generally normal, but may be somewhat flaccid and discoloured. In the *brain*, when death has occurred after cerebral complications, the membranes are congested, and when stripped off reveal the gray substance darkened by pigmentation; there is sometimes subarachnoid effusion. A similar alteration may be found in the spinal cord, which probably accounts for the occasional cases of partial paralysis which follow malarial poisoning. In the bones the marrow is also discoloured by pigment.

In the *chronic infection* the alterations are more marked and varied than in the acute form. The *blood* is diminished in quantity; it contains more water, and pigmentation is not so pronounced as in the acute form. The proportion of white and red corpuscles is altered; some authorities say that the former have increased, while the red cells have relatively diminished. The *spleen* is generally enlarged, and becomes hardened and friable, the pulp is increased, and the capsule and trabeculæ become somewhat thickened, and tough and inflammatory products may accompany the hypertrophy. The normal weight of 5 to 7 oz. increases to as many lbs., and even 18 lbs., 20 lbs., or more have been recorded. On the other hand, it has been found atrophied, weighing as low as 1 oz. 19 grs. (Russell, 51). In the enlarged state, especially when softened, as it sometimes may be, it is easily injured, and is frequently the cause of fatal accidents. Indeed, among the natives of India it is sometimes ruptured by slight blows or falls, or even "spontaneously." In some cases a state of contraction of the fibrous elements—fibrosis—may be induced, the structural change becoming permanent. In this diseased condition of the spleen leucocytosis and anæmia are well marked. The splenic veins are engorged with blood containing pigment and the débris of parasites or cells; pigment is found also in the connective tissue.

The *liver* may be chronically congested, indurated, and enlarged from interstitial deposits, and this may terminate in cirrhosis; it is dark in colour and marked with pigment. In this condition its functions are interfered with, and various complications result. Acute inflammation of the liver seldom occurs in this state, but it does sometimes suppurate insidiously. The *kidneys* are sometimes found to be the subject of chronic nephritis and inflammatory congestion.

When pneumonia has occurred the *lungs* are congested or hepatised, the seat of local hæmorrhages and, in portions, of fibrosis. The heart may be flaccid and the cavities dilated; firm fibrinous coagula are found in some cases, which extend into the pulmonary artery; but other changes are probably accidental, and not due to malaria further than has been previously narrated.

The mucous membrane of the *gastro-intestinal* tract may be found chronically affected; the stomach and duodenum are most prone to suffer; disease may occur everywhere throughout the tract. It may be remarked that the anatomical structure of the lower end of the ileum favours tension during congestion, and consequently ulceration; this may explain the pathological changes attributed to enteric fever, either specific or typho-malarial. In cases complicated with dysentery, which is common enough—as some would say, only another form of the same disease—ulceration and thickening in various stages are found in the large gut: but they extend sometimes beyond the ileo-colic valve into the ileum.

where ulceration of the mucous membrane and Peyer's patches resembles that of specific enteric fever.

With regard to certain changes which point to the implication of the *nerve centres*, it was suggested by Frerichs that these might be due to plugging of the small vessels by pigment. Laveran points out that if these thrombi are formed of parasitic elements, and not of inert pigment matter, they may be dissipated in certain cases, and the symptoms pass away; thus transitory aphasia and paralysis, produced sometimes during paroxysms of fever, are explained by temporary obstructions limited to certain vascular areas of the brain. The presence of hæmatozoa in the cerebro-spinal nerve centres furnishes a satisfactory explanation of the nervous symptoms, such as cephalalgia, rachialgia, delirium, convulsions, coma.

How far the various pathological conditions are the result of the mechanical action of the hæmatozoa in obstructing the circulation, or of their effect in altering and disorganising the blood corpuscles, or in the production of a toxic agent, we are hardly in a position to determine. It is possible that the effects may be a result of a combination of all these conditions.

Treatment.—It is needless here to dwell on the spoliative and heroic forms of treatment practised in past times, which to a certain extent were advocated by high authorities up to the times of Twining, Mackintosh, Annesley, and others. Since then bleeding and mercurialisation have given place to a milder, more rational, and more effective mode of treatment.

An ordinary attack of intermittent fever is generally treated as follows:—The bowels are thoroughly relieved by an aperient of colocynth, calomel, blue pill, or compound jalap, followed by a saline aperient, consisting of sulphate of magnesia and soda, with 2 or 3 grs. of quinine and some bitter infusion; this it may be expedient to repeat for two or more days, and perhaps subsequently. Thus is relieved not only constipation, but the congested condition of the abdominal viscera and portal circulation. If there should be signs of gastro-intestinal irritation, coated tongue with red edges, and if there be a tendency to diarrhœa and dysentery, one or two doses of 15 to 20 grs. of ipecacuanha may be substituted for the aperient. During the cold stage warm drinks, warm clothing, and hot bottles are needed. During the hot stage cooling drinks, ice to the head if it be hot and painful, and the following diaphoretic may also be given:—℞ Liquor ammon. acet. ℥ij.; Sp. ether nitros. ʒij.; Potas. acet. ʒij.; Mist. camph. ℥vj. M. One-eighth part every two or three hours.

In the sweating stage rest and quiet are necessary, care being taken to avoid chills. Quinine should now be given and repeated every three or four hours in the following form:—℞ Quin. sulph. *vel* hydrochlor. grs. xl.; Acid. sulph. dil. *vel* Acid. hydrochlor. dil. ʒj.; Tr. aurantii, ʒij.; Aqua, ℥viij. M. One-eighth part for a dose.

The diet should be light, and stimulants, unless there be some special necessity, are not required. During the intervals the patient should avoid fatigue, excitement, chill, or other exposure to vicissitudes of weather; and should continue to take quinine, after the first three or four doses, at longer intervals, say of six hours, until cinchonism begins to appear, when it may be gradually laid aside. Before a second or third attack occur, it is well to take a dose of 5 grs. of quinine about one hour before the onset, and if the first dose of 5 grs. have not postponed or diminished the paroxysm, 10 grs. may be given. Some give 10 or 15 grs. at first, but five will generally suffice in ordinary cases. The dose may subsequently be reduced to 3 grs. and given at longer intervals. It is necessary to keep the bowels open, not merely with the object of removing accumulation, but of relieving the portal system, liver, and spleen. A method that used to be, and perhaps is still practised in Bengal, was to give 40 grs. or a drachm of compound jalap powder with 2 grs. of calomel, at the outset, to be followed by the quinine. Quinine will have less effect without it; with it, it is most efficacious in diminishing the intensity and in many cases preventing the return of fever.

In uncomplicated cases of intermittent fever this method of treatment will generally be efficacious and sufficient. If in spite of this there are persistent recurrences of fever, larger doses of quinine or arsenic will be needed; in which case Fowler's solution, in doses of 5 to 6 minims thrice a day, may be used.

In the treatment of remittent fever and its complications antiphlogistic measures are as inappropriate as in intermittent. The bowels should be freely acted on by colocynth or jalap, with a moderate dose of calomel and saline aperients, as necessary. Diaphoresis should be induced as before, or antipyrin or phenacetin may be useful. Cooling drinks and iced water should be given; ice may be applied to the head—which should be shaved or the hair cut short—if the pain or heat be great. Cold affusions, sponging of the body, or even the wet sheet may be used if the temperature be very high. Draughts of tepid water will soothe the stomach and relieve it of bile or other matters; and, if vomiting or retching be obstinate, swallowing small pieces of ice is grateful. Effervescing draughts, with citrate of potash or iced soda water, the application of a sinapism, or chloroform on a piece of lint over the stomach, will sometimes relieve the nausea and pain. Hepatic pain may be dealt with by hot fomentations, and very occasionally a few leeches may be necessary.

A most important indication is to watch for any symptom of remission: this generally occurs in the morning, being indicated by decrease of suffering and the presence of cutaneous moisture; then a full dose of quinine of 10 to 15 grs. should be administered: 20 grs., even 30 grs. are sometimes given, but it is doubtful whether they are better than the smaller dose. When the stomach will not retain the quinine, it should be given hypodermically or by enema, the former method being the better. With due precautions there is little danger of local mischief, though abscess, sloughing, erysipelas, and even tetanus have followed this operation, probably when such precautions have not been observed. Where the splenic cachexia is marked, it is well, if possible, to avoid this operation. Quinine must be continued until the remission becomes more perfect, the tongue cleans, and the prostration diminishes. Large doses need not be continued, but enough to keep up a moderate degree of cinchonism.

When the fever assumes the adynamic form and becomes continued; when typhoid symptoms are setting in with delirium, sordes of the tongue and lips, tremor of muscles, depressed cardiac action and feeble pulse; or, on the other hand, when the febrile condition assumes the sthenic type, and no sign of remission appears, quinine in 10 gr. doses, or, according to some, 15 grs. or 20 grs., should be given irrespective of the remission. Pyrexia does not contra-indicate the administration of quinine, which often reduces temperature and produces marked improvement. High temperature, a coated tongue, and even constipation need not prevent its employment in a bad case, though the bowels should be relieved as early as possible. When the adynamic state supervenes, in addition to the quinine, brandy and other stimulants are necessary; they may be given in combination with a decoction of cinchona and ammonia. The amount of alcohol will depend on the state of the pulse.

As to diet, animal broth, milk and similar nutrients are necessary, and must be given frequently and in small quantities. Convalescence must be carefully tended, and change of climate enjoined as soon as the strength is sufficiently re-established to enable the patient to take a voyage.

The essential principles of the treatment are to keep the bowels open (not purged), to relieve visceral engorgement, reduce the temperature, and neutralise the poison. Nothing so well fulfils these indications as quinine, and the most marked effects are shown in its influence on grave forms of malarial fever. Its action as a crucial test of malaria is significant but not absolute; for it will reduce the temperature in continued as well as in paroxysmal fevers. In the most fervent of all fevers, the ardent or thermic, when the temperature rises so high as to imperil life, hypodermic injection of quinine appears to have the power of reducing it, and it is now given in other fevers with this object.

In the pernicious attacks of malarial fever, when the algid, gastro-intestinal, cerebral or dyspnœal symptoms supervene, quinine must be combined with stimulants in free doses and warmth. In the cold stage it may sometimes be advantageously combined with opium; and warmth should be applied to the body generally. When coma supervenes in the hot stage there should be free purgation; ice may be applied to the head, sinapisms to the legs and trunk, and stimulating enemas, in which 30 grains of quinine may be dissolved, or a hypodermic injection of from 5 up to 10 grs. may be administered: a few leeches to the mastoid processes may also be useful; blisters are sometimes applied to the nape of the neck. Under the influence of quinine the symptoms may subside and the fit terminate favourably. Very high temperature with congestion and stertor suggest active measures, as above described. The latter condition may be mistaken for apoplexy or insolation.

When the algid condition occurs, as already stated, warmth and quinine are required; and it is in this condition, especially when there is gastralgia and vomiting, that opium affords relief.

It is perhaps right here to allude to the remedy known as the tincture of Warburg, which possesses febrifuge and diaphoretic properties in a remarkable degree; but there is probably no valid reason for preferring it to other preparations of quinine. Dr. Maclean and others speak highly of it, and, as its composition has been declared, this objection to its use has been removed.

In the treatment of malarial cachexia, with enlarged liver and spleen, the most important points are change of climate and the judicious use of preparations of iron and quinine; bearing in mind the necessity for relieving portal congestion before full benefit can be anticipated from other remedies. Depletory measures or purgation are not required; but gentle action by saline laxatives such as before mentioned, combined with quinine, iron, and vegetable bitters, such as calumba, is desirable. A carefully regulated and nourishing diet and protection from all vicissitudes of climate must be enjoined. In these cases benefit may be derived from the saline and ferruginous waters of various health resorts, and from such measures as tend to preserve the general health. A prolonged absence from the country in which the mischief originated, and residence in a more bracing non-malarial climate, are necessary.

In the treatment of the splenic form of cachexia with the chronically enlarged spleen that gives rise to it, the use of iron is essential. Any of the more soluble preparations of iron are good, but perhaps none is better or so good as the sulphate of iron with quinine, in the following formula for example—℞ Ferri sulph. grs. xvj.; Quinæ sulph. grs. xxiv.; Acid sulph. dilut. ʒj.; Sod. sulph. ʒij.; Tr. myrrh. ʒij.; Infus. calumbæ, ℥viij. M. Two tablespoonfuls twice a day. Or as a laxative to be taken in the early morning—℞ Mag. sulph. ℥j.; Sod. sulph. ℥j.; Tr. myrrh. ʒij. Aq. menth. virid. ℥viij. M. Two tablespoonfuls in the early morning, 6 or 7 A.M.

The old form of administration, known as the spleen mixture, used in Bengal many years ago is very efficacious. Twining (57) gives it as follows:—℞ Pulv. jalap, Pulv. rhei, Pulv. calumbæ, Pulv. zingiberis, Potassæ supertartratis, āā ʒj.; Ferri sulphatis, ℈j.; Tinct. sennæ, ʒiv.; Aquæ menthæ sativæ, ℥x. Misce. One-tenth part twice a day.

In these conditions the use of mercury, except perhaps as an alterative dose, is especially to be deprecated; with the exception that the local application of the red iodide of mercury as an ointment, which has been found effective in reducing an enlarged spleen or goitre, may be resorted to; a small piece about the size of a marble being rubbed in over the organ while it is exposed to the direct heat of the sun or fire.

The rest of the treatment consists in the use of tonic remedies, occasional laxatives, a well-regulated and nourishing diet, with a certain amount and such form of wine, or other alcoholic stimulant, as may be most suited to the particular case. A perfectly quiet, uneventful, and well-regulated life, a very moderate amount of exercise, and warm clothing, should be advised; and chills, fatigue, and violent stress of any kind, physical or emotional, avoided. Neglect of these precautions may be attended by cardiac failure, death from fatal syncope or from intravascular coagulation. Of the numerous other antiperiodics that are used in the treatment of malaria none is comparable to quinine in its various forms.

Quinine.—The salts of quinine possessing aseptic, antiperiodic, antipyretic and parasiticidal properties, are specially indicated in the treatment of all forms of malarial infection.

The acid hydrochlorate is the most soluble of the salts of quinine, and is therefore the best for hypodermic injection. The acid hydrochlorate is soluble in 0·66 of water. A solution of equal parts by weight of acid hydrochlorate and distilled water is recommended, as it produces no irritating effects except some pain. Triulzi (30) says that the addition of half a part of antipyrin to one part of basic hydrochlorate makes it soluble in two parts of distilled water at a temperature of from 77° to 86° F. Laveran says that this solution causes less pain than the acid hydrochlorate, and is as effective. A solution of Quinine sulphate, one part, Acid. tart. half a part, Water, ten parts, makes also a good form of hypodermic injection, and is used frequently in India. The quantity of either of these solutions should be enough to contain five to ten grains of the salt. Care must be taken in introducing the solution that the point of the needle shall have passed through the skin well into the areolar tissue, and that it be directed away from the skin before the fluid is injected. The solution should be perfectly clear, free from crystals or foreign matters; the needle and syringe should be made aseptic before use. Hypodermically taken, quinine is more efficacious than when taken by the stomach, and five to ten grains are full doses. When ten grains are necessary, it would be better to give it in two injections in different parts of the body.

The form most frequently adopted as a draught is the sulphate. This requires an acid for its solution. Grains xx. of this quinine require 20 drops of dilute sulphuric acid to dissolve it. It contains 74 per cent of quinine. The neutral sulphate is more soluble in water, and may be prescribed without acid; it contains 59 per cent of quinine. The hydrochlorate contains 81 per cent of quinine, and is soluble in water. A little dilute hydrochloric acid may be added when the basic salt is used. Quinine is given most effectively in solution; but, when from any cause it cannot be so taken, it may be given in powder suspended in water, in cachets, tabloids, rice paper or in pills; the last is the least satisfactory method, as the pills when swallowed are sometimes not dissolved.

In ordinary cases of fever two to five grains given by the mouth are generally sufficient, three or four times in the day. In more serious cases ten or even fifteen grains may be necessary, and possibly in very urgent cases as much as twenty grains; but more than this I consider is not required, and may cause toxic symptoms.

Where administration by either stomach or hypodermic injection is difficult, the acid hydrochlorate or sulphate may be given in an enema.

The old method of administering by absorption through the skin from a blistered surface is obsolete.

The possible danger of tetanus after hypodermic injection must be borne in mind; but if aseptic precautions be taken, and if the solution be injected under, not into the skin, the risk is minimised. The non-irritating solution when thus carefully injected seldom causes any after-trouble, though occasionally a small abscess may form. The hypodermic method is the quickest and most effective way of exhibiting the drug; and in serious cases, especially in the pernicious or typho-malarial forms, and in severe thermic fever, and when, as sometimes happens, the stomach is unable to tolerate or retain it, it should be so given.

The mixed alkaloids, or quinetum, may be used in milder cases of malarial fever in the same doses as the sulphate of quinine, but they are not so much to be depended on.

There are other salts of quinine, such as the citrate, hydrobromate, lactate, salicylate, but they are inferior in therapeutic value to the forms already named. The preparations of the cinchona bark, which at one time were so much used, have ceased to be employed since the separation of the alkaloids, except occasionally with ammonia in adynamic fever.

Arsenic is also a febrifuge and antiperiodic. Sometimes when quinine fails, arsenic will succeed, in doses of four or five drops of the liquor arsenicalis twice or three times a day, always after meals; or it may be given as the liquor hydrochlorate of arsenic (five drops) combined with hydrochlorate of quinine (two or three grains) in the same way. In the earlier condition there is no reason to think it is ever better than quinine; but in the chronic condition of malarial poisoning, with frequent returns of fever, neuralgia, or other indication of its chronic action, benefit frequently arises from the use of arsenic in the above small doses, continued for protracted periods of some weeks, with intervals of omission of three or four days after every ten days. It seems to aid in restoring the integrity of the digestive processes, in giving tone to the nervous system, and favouring nutrition by its effect on metabolism. Care must be taken not to continue it so long as to set up symptoms of gastric irritation; if this begin to appear, or if the eyelids begin to feel irritable, it should be discontinued for some time.

The antiperiodic powers of opium and its alkaloids are probably a prominent reason why opium eating and smoking have become so widespread among the inhabitants of India and China. In the earlier stages of malarial fever, especially in the asthenic conditions in which that disease occurs in so many of the inhabitants of India, it gives great relief, soothes pain, breaks or arrests the periodic returns of fever, and seems to assist those exposed to malarial influences in resisting them. For this purpose it has been used ever since the time of Galen. Trotter, Lind, and others prescribed it. It would probably be hurtful during the hot stage, but during the cold and sweating stages it might be beneficial. Waring says that he has seen it cut short the cold stage like a charm, and mitigate the severity of the following hot stage. Only in exceptional cases of malarial fever is it likely to be used, as there are so many other febrifuges that would better fulfil the purpose; but no doubt the relief it is capable of affording explains the estimation in which it is held by the natives of India. Sir W. Roberts (49*a*) suggests that the antiperiodic alkaloid may be anarcotine.

Methylene blue has recently been recommended as an antiperiodic and febrifuge remedy; and experiments by Rosin and others seem to show that it is an active germicide: there is no evidence, however, to show that it is superior or equal to quinine.

Many other drugs have been recommended, but they are inferior to the cinchona alkaloids. Such are biberine, salicine, strychnine, atees (the native name for *Aconitum heterophyllum*), piperine, ilicine, bonduc nut (the fruit of *Cisalpina Bonducii*); salts of iron or zinc, nitric acid, the hypophosphites, alcohol, and a large variety of native drugs. These, or some of them, especially iron, may be of service in certain stages of fever or in the splenic cachexia following it. Atees is much used.

Prophylactic measures may be personal or general.

As in all malarial countries some seasons are more unhealthy than others, individuals and bodies of men should, if possible, select the healthiest seasons for travelling or other exposure to the atmospheric influences; and at all seasons the notoriously malarial sites should be avoided, especially at night. Purity of drinking-water ought to be the subject of the greatest care; that of springs and running streams should be used if possible; under all circumstances, but especially if taken from wells or other such sources, the water should be filtered and boiled before drinking.

The upper floor of a house should be chosen for sleeping-apartments if possible. The ground itself should never be slept upon, or if this cannot be avoided a waterproof should be placed between the body and the ground. Whatever might debilitate or exhaust should be avoided. Food should be good, nourishing, and sufficient in quantity; a certain amount of stimulant, according to habit, may be taken, but all excesses should be avoided. Tobacco smoking in moderation is not hurtful to those who are accustomed to it. Tea and coffee are good prophylactics. In the early morning when travelling, or in malarial seasons, three to four grs. of quinine should be taken. The head should be protected from the sun, the body from over-fatigue.

Persons who have suffered previously from malarial fever, or who have any affection of the spleen, or cachexia, should be doubly careful to observe the above precautions. It may here be repeated that such persons should most carefully avoid exposure to chill, mental or physical fatigue, and errors of diet, as nothing is more likely than these to produce a recurrence of the disease.

In sleeping-apartments the windows should be kept closed on the side to which marshes or malarial localities lie to windward. It is well not to sleep under trees or in the open air, if it can be avoided; a mosquito curtain should be used. The clothing next the person should always be woollen, however light.

As to general prophylactic measures: stagnant subsoil water is a fertile cause of malarial fever, drainage is therefore one of the most effective prophylactic remedies. The draining of marshes, the making of canals, railway cuttings, roads, embankments, fortifications, and such like, and the cutting down of jungle, should be executed with great precautions, and if possible at the most healthy seasons: the labourers are to be protected by proper shelter, removal from the seat of labour at night, and the free use of quinine and proper diet while they are at work. Though the breaking up of the soil may be attended with danger, the subsequent cultivation and cropping is followed by the most advantageous results. The planting of trees—the eucalyptus especially—is beneficial. The good results of the action upon soil and air of the growth of these trees appear to be well established.

Resting-places and camps should be placed on the highest available ground, away from marshes or damp ground, or on the high banks of a running stream. In encampments large fires should be burned at night. Perfect drainage and the removal of organic matter from the vicinity of dwellings, sufficient air-space in sleeping-apartments, thorough ventilation, and perfect cleanliness are of the utmost importance.

Purity of water-supply has been found one of the best of all prophylactics in the protection of the community from malaria.

SECTION IV.—INDIAN ENTERIC FEVER

Etiology, Prevalence, and Communicability.—Enteric fever occurs all over the world, from the arctic to the torrid zone; it is generally held to be of specific origin, and in this respect independent of climatic influences. The various characteristic phenomena and lesions presented by it are considered to be due to the action of the bacillus discovered and described by Eberth, Gaffky, and others, which distinguishes it etiologically from all other continued fevers, and confers on it specific characters and aptitude for communicability.

About forty years ago it began to be suspected that certain forms of fever in India, hitherto regarded as malarial or climatic, were identical with typhoid. Further observation in different parts of India has confirmed this view, and it has now come to be acknowledged as the chief cause of fever mortality amongst young soldiers and others—Europeans or natives—of like age. There is no reason for supposing that it is a new disease; but more accurate observation of symptoms and pathological lesions has led to its distinction from other fevers with which it had been confounded.

Enteric fever presents a greater severity, prevalence, and diversity in tropical and subtropical than in temperate climates; to this India offers no exception, for it prevails throughout that country. But there is reason to believe that cases having very similar symptoms and pathological lesions may result from different causes. For amongst other evidence it appears that young persons, especially those under 25 years of age, exposed to the action of malaria, even on ground never before occupied, and where the drinking-water is free from fæcal contamination, may suffer either from the simplest febricula, ague or remittent, or from fever having all the symptoms and lesions of the enteric form, or from remittent fever with typhoid symptoms in which the enteric lesions are absent.

Whatever may be true elsewhere of the nature and etiology of the specific form, no doubt holds good in India; but it should be borne in mind that the universal prevalence of malaria must be regarded as a disturbing element, and that there are cases not distinguishable from specific enteric which may be traced to a malarial or miasmatic origin; whilst the course of specific enteric itself may be modified by malarial action. Indeed, cases to which the term typho-malarial has been given are probably due to this combined action. As the symptoms and lesions of enteric fever do sometimes supervene when the possibility of fæcal contamination seems to be excluded, the inference appears justifiable that malarial fevers can induce like pathological changes. There are no valid grounds for asserting that ulceration in the ileum and Peyer's patches are the result only of a single cause. [*Vide* art. "Scarlet Fever," Sect. Pathology, p. 166.—Ed.]

Provisionally speaking, then, two forms of fever with enteric symptoms and lesions may perhaps be admitted:—(i.) The specific enteric fever or typhoid; (ii.) Malarial or tropical enteric or typhoid; the distinction of one from the other being difficult and not always practicable. Of course it is quite possible that other forms, the result of the action of both poisons, or of pythogenic and miasmatic causes combined with heat and other climatic influences, may occur.

An example in my experience was presented some years ago in the case of a healthy European lad of about 18 or 19, who was prostrated suddenly with thermic fever after direct exposure to great heat. High fever was followed by enteric symptoms and lesions, and a fatal result in about three weeks or a month. It is impossible to affirm that a specific bacillus did not here take part, but there were no special grounds for asserting that it was so. In other cases of malarial remittent contracted in India and sent home for change, the characters of enteric fever have gradually supervened and ended fatally. For such, an explanation may be found in the views expressed by some observers, and especially by Léon Colin (11*a*), who says: "Elle tient surtout à la transformation dans l'individu lui-même de fièvre malarienne qui infecte l'organisme et met celui-ci en puissance de créer la fièvre typhoide par autoinfection."

It is fortunate that, while we wait for further information, experience has taught that prophylaxis depends on pure air, pure water and sound hygiene; and that the therapeutics of both forms of fever are practically the same. The following statistics, which are taken from the report of the Sanitary Commissioner with the Government of India for 1892, show the prevalence and mortality from enteric fever in the European and native armies:—

TABLE.—Seasonal Prevalence of Enteric Fever in the European Army in 1892 (Admissions into Hospital).

	January to March.	April to June.	July to September.	October to December.
1. Burma Coast and Bay Islands	...	3	3	...
2. Burma Inland	...	1	14	3
4. Bengal and Orissa	2	3	1	7
5. Gangetic plain and Chutia Nagpore	47	44	36	50
6. Upper Sub-Himalayan	66	104	54	137
7. Indus valley and N.W. Rajputana	12	38	32	6
8. S.E. Rajputana, Central India, and Gujerat	14	40	39	30
9. Deccan	37	36	116	29
10. Western Coast	2	1	1	3
11. Southern India	15	14	20	3
12A. Hill Stations	7	126	165	33
12B. Hill Convalescent Depôts	...	33	24	2

The hill stations and the Deccan give the largest returns. The third quarter of the year shows the highest mortality.

TABLE.—Enteric Fever in the European Army in the Decennium 1882–1891 and in 1892.

Stations over 1000 *strong.*

Stations.	Decennium 1882–1891.		Admission-rate per 1000 of Strength in 1892.	Death-rate per 1000 of Strength in 1892.	Died out of each 100 Cases treated in 1892.
	Admission-rate.	Death-rate.			
Bareilly	34·2	8·67	44·4	16·86	28·79
Lucknow	32·7	5·62	29·6	6·45	16·67
Sialkot	32·1	8·13	52·4	9·87	16·25
Kurrachee	22·4	4·00	23·7	3·79	16·00
Rawalpindi	19·9	5·34	26·8	8·69	27·91
Secunderabad	19·4	5·40	23·5	5·33	21·74
Mhow	19·2	5·31	13·9	1·89	12·50
Meean Meer	19·0	5·75	14·7	5·88	37·50
Bangalore	18·1	3·66	17·0	2·06	9·30
Meerut	15·9	4·93	23·0	6·18	19·64
Quetta	14·0	3·67	30·7	3·62	11·76
Agra	13·9	4·46	15·5	6·01	38·89
Umballa	10·6	2·49	21·9	4·69	18·00
Poona	10·5	3·58	31·0	9·14	26·87
Peshawar	10·4	4·33	11·0	5·49	47·37
Colaba (Bombay)	4·6	1·59	4·9	1·95	40·00
Fort William	3·7	2·21	2·7	...	...
Belgaum	2·9	1·19	1·8	·90	50·00

Statement showing the Death Ratios of the European Army from Enteric Fever at different Periods of Residence in India, together with the Ratios of Liability to it.

Year.	1st and 2nd Years.		3rd to 5th Year.		6th to 10th Year.	
	Deaths per Mille.	Percentage of Liability.	Deaths per Mille.	Percentage of Liability.	Deaths per Mille.	Percentage of Liability.
1889	11·65	57·02	4·20	20·56	2·43	11·89
1890	10·21	66·47	2·98	19·40	2·17	14·13
1891	11·60	64·19	3·64	10·14	2·23	2·34
1892	10·69	65·99	3·6	20·74	2·15	13·27

Statement showing the Death Ratios of the European Army from Enteric Fever at different Ages, and the Ratios of Liability to it.

Year.	24 and under.		25 to 29.		30 to 34.	
	Deaths per Mille.	Percentage of Liability.	Deaths per Mille.	Percentage of Liability.	Deaths per Mille.	Percentage of Liability.
1889	9·81	64·50	3·25	21·37	1·83	12·03
1890	7·78	65·93	2·84	24·07	1·18	10·00
1891	9·11	68·65	2·97	22·38	·71	5·35
1892	8·44	64·87	2·92	22·44	1·65	12·68

The last two tables show how far age and length of service in India determine the incidence and mortality from enteric fever, the ages 24 and under being three times more fatal than 25 to 29; whilst the first and second years of service are much more fatal than the third and fourth, and so on with increase of age or length of service.

Bryden, in his *Statistical History of the European Army in India up to* 1876, says enteric fever has no geography—no regiment or battery escapes it in the first year, whatever cantonment may be selected. He gives the following analysis of 368 deaths:—

Age.	Deaths.
24 and under	255
25 to 29	90
29 „ 34	17
35 „ 39	4
40 and upwards	2

Seventy-five of these deaths occurred within three years after landing in India, and 94 per cent of the total were under thirty years of age.

Admission and Death-rates per Mille from Enteric Fever in the European and Native Troops and Jails of India compared.

	1882–1891.		1892.	
	Admissions.	Deaths.	Admissions.	Deaths.
European troops	14·7	4·13	22·1	5·52
Native troops	·3	·09	·4	·13
Jail population	·2	·10	·3	·15

Mortality from Enteric Fever of Native Troops compared with European Troops in 1892.

Died per 1000 of Average Strength.		Relative Liability in Percentages.		Percentage in Deaths from all Causes.	
European Troops.	Native Troops.	European Troops.	Native Troops.	European Troops.	Native Troops.
5·52	·13	97·7	2·3	32·3	·8

In the whole native army of India 54 cases with 16 deaths were returned as enteric fever in 1892, as against 35 with 17 in 1891; 14 of the deaths were in the Bengal, and 2 in the Bombay army.

This apparent rarity of enteric fever in the native army may be explained by the probability that cases have been recorded under "other fevers" which should have been classed as enteric; but another reason is the nature of the food, for it would appear that whilst meat-eaters (the Europeans, for example) are especially prone to it, the ordinary sepoy, whose diet consists chiefly of rice or wheat, suffers least of all; certain races which have a mixed diet, including meat (Gurkhas, for example), suffer more than the grain-eating sepoys, as seen from the following table:—

Admission and Death-rates per Mille from Enteric Fever in the European Army, Native Army of Bengal, and Gurkha Regiments, 1888-1892.

	Admissions.			Deaths.		
	European Army.	Native Army of Bengal.	Gurkha Regiments.	European Army.	Native Army of Bengal.	Gurkha Regiments.
1888	13·6	·1	1·0	3·75	·10	·38
1889	22·9	·3	1·0	6·11	·09	·50
1890	18·5	·2	·1	4·91	·09	·13
1891	20·4	·3	·1	5·73	·14	...
1892	22·1	·7	2·3	5·52	·21	·76

Whatever the origin of enteric fever, there can be no doubt that its prevalence, course, development and symptomatology largely depend upon external as well as personal conditions; and, as has elsewhere been stated, the affinities between all forms of tropical fevers, various though their manifestations may be, are probably closer than is generally supposed. An exclusive application of theories which are appropriate in Europe may not be justifiable in India, and it seems possible that the disease may have other sources of development in India. With Léon Colin (11*b*) I am of opinion that all acute febrile conditions, accompanied by an alteration in the secretions and by gastro-intestinal complications, may induce the ulceration of Peyer's patches, and that it may be impossible to recognise the affection during life; the remittent fever, for example, being transformed into "typhoid."

If it be asked why any other explanation than that accepted in this country be sought, the reply is that in India the facts are not covered by that explanation, for there is as much or more evidence that other fevers may assume the enteric condition as that all forms of enteric fever are caused by a specific bacillus.

Annesley, Twining, Morehead, and others had, long before Scriven, in the case of the Europeans, and Ewart in the case of the natives, pointed out the existence of diarrhœa and enteric ulceration in adynamic forms of fever.

Annesley says: "Marks of disease of the small and large intestine are confined to their internal tunics; the small intestine, especially the duodenum and the termination of the ileum, is very frequently diseased on its mucous surface, which is inflamed and studded with small ulcerations. In a few cases perforation of the bowel supervened."

Twining, in 1842, says: "In instances where patients have died after protracted fever, superficial ulcerations of the mucous membrane of the small intestine were found." The general characters of this congestive fever, as he calls it, are similar to European typhoid.

Martin (27) refers to intestinal ulceration in neglected fever of from twenty to fifty days' duration. Dr. Morehead, in a letter to me, says he agrees in thinking that Peyerian ulceration is not necessarily the product of one cause, or associated with one set or order of symptoms.

Dr. John Macpherson writes that at the General Hospital of Calcutta, before 1850, he observed ulcers of Peyer's patches, and was reminded of dothienenteritis, which he had seen in Edinburgh.

In 1854 I described a case in a young man of 28 years of age, who died after a fever of more than three weeks' duration, attended with diarrhœa, hæmorrhage from the bowels, iliac gurgling, tympanites, stupor, sordes, and collapse supervening on perforation. He had been exposed to malarial influences, and was considered to be suffering from malarial fever. There was no reason to suppose he had been exposed to fæcal poisoning, though, of course, it is impossible to prove the negative.

Dr. Maclean, C.B., says he treated fevers in Secunderabad and in China, with intestinal lesions and frequently death from hæmorrhage; these he considers to have been enteric.

Dr. Gordon, C.B., says he saw British soldiers with enteric complications that could not be traced to any pythogenic or specific origin.

Dr. Chevers says: "If we insist upon calling a case of paludal remittent with bowel complications true enteric fever, and withhold quinine, the case will almost inevitably end with death."

Dr. Alexander Smith, A.M.D., says in 1873: "With the setting in of the rains in June or July the fevers assume more of the remittent and continued types, running a slower course, and showing in an unusually marked degree in the latter form the bowel complications said to be characteristic of enteric or typhoid fever."

Dr. Wall, of the General Hospital, Calcutta, writes (in a letter to me): "I have seen many cases that could not with certainty be referred to any type of fever, but resembled remittent more than any other, and in which intestinal ulceration was found after death."

Professor M'Connell, of Calcutta (in a letter to me), writes of "enteric fever" in India: "I am inclined to believe that the evidence of a specific poison is not nearly so generally available here as in Europe; that probably climatic influences, *plus* want of proper sanitation, give rise to it in India, that in not a few cases the etiology seems to differ from that assigned to it in Europe, namely, specific fæcal contamination, and that it may possibly arise from climatic causes, combined with non-specific fæcal evacuations or other poisonous material, the result of an insanitary condition of dwelling-houses, cesspools, drinking-water and other sources of contamination."

Dr. Alfred Clark, A.M.D., writes: "Some hold that a specific poison or germ is not absolutely a *sine qua non*, but that ordinary filth causes may develop it *de novo*; the climatic influences acting on young, undeveloped constitutions may start the disease. I have seen genuine enteric fever in India, where all filth causes, in the general meaning of the term, were absent."

Dr. W. B. Beatson, I.M.S., writes: "I think that remittent fevers in India often imitate typhoid, and are described as such."

Dr. Oldham, I.M.S., writes to me: "There is a great deal of fever in India of purely climatic origin, which so closely resembles enteric fever as to be distinguished from it with difficulty."

Dr. Whytlock, A.M.D., reporting on Peshawar, says: "The miasmatic disease of that place is particularly prevalent at all seasons, but more especially in September and October. Ague prevails to an enormous extent; the early and late cases assume all the appearances and symptoms of cholera. There is every range of fever, from ordinary intermittent to remittent and typhoid."

Dr. Woodward of the U.S. army says the malarial influence and pathological processes to which it gives rise are not merely manifested by the frequency of ordinary ague. A Board of Inquiry reported that while a certain number of cases of ordinary typhoid existed in the army, the large majority were bilious remittent, which assumed the adynamic type prevalent in enteric fever. He believes this form of fever to be due to the combined influence of malarial poisoning and the cause of typhoid fever, and proposed the term typho-malarial.

Professor Sims, of Memphis Medical College, America, speaking of typho-malarial fever, says: "The gut pathology exists in a smaller percentage than in typhoid, which in typho-malarial fever is probably due to pathological changes, the result of long-continued exposure to malarial influences."

Professor Dickson, of America, says: "On examination, typhoid lesions will be sometimes found in the body of a person dead of bilious remittent."

M. Léon Colin says it was abundantly shown in Algeria and Italy that malaria confers no immunity as has been supposed from typhoid fever, but that intermittent and typhoid appeared simultaneously in the same regiment.

Dr. J. Wise, I.M.S., who studied fever for many years, in a letter to me speaks of remittent fever with enteric symptoms, and unreservedly expresses the opinion that enteric fever may be of malarial origin.

Dr. Parkes entertained doubts that the generally accepted cause is the only one to which enteric fever is to be referred.

Dr. Bryden says: "I made the generalisation that the typhoid fever of British soldiers in India is primarily due to climatic influences."

Dr. Hoystead, I.M.S., in a letter to me, writes of the close affinity which exists in India between pernicious remittent fever and typhoid.

Dr. Maclean, R.N. (in a letter), alludes to the occurrence of enteric fever in the island of Ascension, under circumstances of close observation, where no connection could be traced with defective sanitary arrangements; though it is probable that malarial influences did occur. He says his investigations utterly failed to connect the fever with any of the conditions commonly believed to be essential to its production. There is no such thing as a drain or cesspool in the island, all the sewage and other filth being removed daily and thrown into the sea to leeward of all dwelling-houses. The water, partly collected from the roofs of buildings during rain and partly condensed, is stored in iron and cemented stone tanks, and removed from all possible sources of contamination.

Bouchard says: "Typhoid is a specific miasmatic fever, and the *materies morbi* not necessarily arising from a previously infected organism may impregnate the air, soil, or water, and may be disseminated by man, by air, by water, and by other objects." He considers the doctrine of a fæcal origin too limited.

Dr. Ryley (in a letter to me) writes from Africa that a fever occurs frequently there having all the characteristic symptoms of typhoid fever as it occurs in this country (Europe); that in no case, though every pains was taken, could he trace the origin of the fever to contagion. That in a few cases the disease seemed to have arisen from the fouling of the drinking-water by excremental matter in a state of putrefaction. In the majority of cases the fever broke out among Europeans first inhabiting or cultivating a virgin soil, the new-comers being most liable to attack, apparently from decaying vegetable matter, paludal emanations, or other climatic causes. It was called a hybrid fever, not because it presented any remission or differed from typhoid fever as it occurs in this country, but because of the difficulty of accounting under the circumstances for true typhoid, according to the views of Budd, Murchison, and others as to its genesis or etiology.

Dr. Johnston Fergusson, A.M.D. (in a letter to me), states his inability to trace outbreaks of this fever to any defective sanitary arrangement.

Dr. Marston, in a report to the Army Medical Department in 1882, says: "I have tried incessantly, and others have done the same, to obtain reasonable proof here (India) of the operation of those causes of enteric fever at home. The more I think of it the more convinced I feel of the inadequacy of this view to account for the facts, or nearly all the facts, as seen in this country." He refers to cases of enteric fever occurring at the military posts in Afghanistan occupied for the first time.

Dr. Manson remarks (34): "It is very evident that the clue to the proper classification of tropical fever has not been found, and I do not think it will be found until investigators disabuse their minds of the idea that these fevers must be modifications or combinations of two poisons only, the typhoid and the malarial. We are too apt to assume that we can assign correctly the various causes of disease, and dislike to think that there are forces and poisons in nature of whose existence we are ignorant. The truth is we are nearly entirely ignorant of a number of specific fevers which from time to time affect the inhabitants of foreign countries. I frequently meet with cases of continued fever, both in foreigners and natives, which do not admit of diagnosis and classification—the Tamsui fever, for example, a disease in which there is continued fever with pains in the limbs, head and epigastrium, an exanthematous eruption, no diarrhœa, and convalescence in twenty days or so. These cases are certainly not typhoid, certainly not malarial."

Dr. Billings of the U.S. army says (4): "In the United States, however, we have many cases of mild continued fever, lasting from twenty to thirty days, which we presume to be typhoid fever, but which are certainly not typical, and which shade into continued malarial forms of fever in a very puzzling way. There are also several known varieties of the typhoid bacillus; and it is not quite certain that one or more of these varieties do not exist at times in the intestinal tract without producing a specific fever in the person bearing them. Can the specific, active, typhoid bacillus be developed from some of these, under certain circumstances, in privy vaults, cesspools or sewage? Is the typhoid bacillus carried in currents of sewer air? Are not all the cases, in which it has been supposed to have been thus carried to affect man, more easily explained in other ways, as, for example, by the supposition that it has been conveyed to articles of food or drink through the agency of flies and other insects? What degree and duration of immunity from subsequent attacks does an attack of typhoid fever convey on man? Is there any difference between the immunity conferred by a mild and that conferred by a severe attack? Are there attenuated varieties of the typhoid organism? Can these be developed into more dangerous forms under certain conditions? Can they be used to produce immunity? All these questions are as yet unsolved, yet probably solvable problems.

The above remarks show that fever with enteric symptoms has long existed in India and elsewhere, and that some at least consider it due to general causes rather than to any specific cause.

Typhoid fever is not considered to be contagious in the ordinary sense of the term, but is communicable through the medium of the alvine discharges, which find entry by the drinking-water or possibly by air in which the micro-organisms are suspended. In the former case contamination is effected by percolation through the soil or other method by which the poison finds entrance into the drinking-water; in the latter case by the desiccation of fæcal discharges that have been exposed to the air, the micro-organisms being carried by the wind or currents of air. The latter explanation has been resorted to when the impossibility of contamination of drinking-water seems to have been established; but however this may be, it is very generally maintained that no case of enteric fever can occur without the presence of one particular bacillus conveyed from one individual to the other. The evidence above cited, however, would seem to throw doubt upon this view.

Incubation.—The incubation period is very uncertain. It has been variously estimated at from ten, fourteen, to twenty-one days, and even much more. On the other hand, it has been said that the disease has appeared very soon after exposure to the cause. From the insidious manner in which it begins, and the uncertainty when exposure may have occurred, the difficulty of defining an exact period is increased; and the uncertainty is as great, if not greater, in India than it is in temperate climates. From eight to fourteen days, perhaps, may be regarded as the average duration, but the period is not indicated by any special symptoms except general malaise, and even that is not always apparent. The onset may be insidious and gradual, or with rigors and other manifestations of the commencement of climatic or malarial fever.

Symptomatology.—The symptoms of ordinary enteric fever, with few exceptions which will be mentioned, are much the same in India as elsewhere, though, as in other diseases, liable to be modified by malarial influences. In India, as in temperate climates, for the first few days there may be only malaise, loss of appetite, slight chills, weariness, and headache. The patient at length lies up; the pulse quickens, the skin becomes hot and dry, there is thirst, heaviness and dulness; the temperature gradually rises within the first five or six days to 104° or more in the evening, remissions occurring towards morning. The splenic dulness is increased, the abdomen becomes distended, with tenderness on pressure, and frequently, but not always, gurgling in the right iliac fossa; diarrhœa of a yellowish pea-soup colour, sometimes flaky, tinged with blood, alkaline in reaction, often occurs, though not so frequently as in temperate climates; the tongue, coated in the centre, becomes red at the tip and edges, cracked and tender. During the second week the characteristic spots may appear, though they are often absent, and on the dark skin of the coloured races are difficult to detect. They are more frequently absent in tropical than in temperate climates. Mosquito or flea bites may be mistaken for them.

As the disease progresses, delirium, at first wandering, becomes muttering and incoherent; the diarrhœa increases, there may be epistaxis or hæmorrhage from the bowels, and in extreme cases subsultus tendinum, muscular twitching, and picking at the bed-clothes. The patient becomes completely prostrated and unconscious, the alvine discharges are involuntary; the tongue is dry, brown and glazed, and the teeth covered with sordes; the character of the pulse does not correspond with the temperature, and is slower than in remittent fever. The temperature rises to 106°, or higher, just before death from exhaustion or from peritonitis or shock caused by perforation of the ulcerated bowel.

The ordinary duration of the fever is from three weeks to a month, sometimes longer. In severe cases it may terminate fatally much earlier, either by the intense action of the poison on the nerve centres, or by perforation of the bowel inducing peritonitis and sudden collapse. In favourable cases the temperature begins to fall, and the tongue to get moist, delirium disappears, diarrhœa ceases, and convalescence sets in in the third week, though it may be considerably later. It not unfrequently happens about the end of the second week that the temperature falls, general symptoms abate, diarrhœa ceases, and appetite and sleep return; the fever is then said to have aborted.

The diagnosis between specific and tropical enteric fever is very difficult, and it is often only by observation of the earlier symptoms, and inquiry into the previous history, that the distinction may be made. In the specific form the invasion is gradual, and it is not for some days that an evening temperature of 103° or 104° is reached. In the other forms the premonitory symptoms are more sudden; chills or rigors are more severe, malaise is greater, the temperature, as early as the first or second day, rises in the evening to 104°, or higher; but even these distinctions are not always well defined: diarrhœa may be absent, and there may be constipation. When ulceration is established, all the other symptoms become identical in both. The eruption is sometimes absent even in the specific enteric; but as it stands in direct relation to bowel ulceration, it may occur, nevertheless, as the latter condition is established. It was noted by Dr. Wise, I.M.S., who gave much attention to the subject among the natives of India, that in the malarial form the stools are acid, and the eyes are always bright and glistening; the peculiar expression of the countenance, characteristic of the specific typhoid patient, being less marked. When enteric symptoms occur in the course of ardent or paroxysmal fevers, when the rise of temperature at the onset is abrupt and the thermograph is irregular, when the nervous symptoms are less pronounced, the origin is probably to be sought in something other than the specific bacillus.

In the course of the disease severe hæmorrhage from the bowels due to opening of vessels during the process of ulceration, peritonitis and collapse the result of perforation of the bowel or of extension of mischief from the ulcerated bowel to the peritoneum, hypostatic pneumonia and bronchial catarrh, thrombosis and plugging of the main arteries or large veins, or even of the right side of the heart or pulmonary artery, failure of the heart's action from weakening of the muscular fibre, may occur as consequences of continued high fever. One or more of these, in addition to hyperpyrexia or excessive diarrhœa, may intensify the danger and cause a fatal result.

That form of the disease in which the symptoms are so mild as to permit of the patient passing through it without being obliged to keep to his bed or even to his room occurs occasionally; but probably less frequently in India than in temperate climates.

Enteric fever in India is very liable to relapse, when the patient may be thrown back into as dangerous a condition or even a worse one than before. The mortality is high, and some of the complications are fraught with extreme danger to life; still there are few, if any, from which patients have not recovered: but whilst recovery will sometimes take place in the worst cases, on the other hand even the slightest can never be considered free from the danger of perforation, profuse hæmorrhage or cardiac failure. A case of enteric fever must always, therefore, be regarded with considerable anxiety, which may continue even for some time after convalescence has apparently been established. Not only may danger arise from sudden accidents, such as those above mentioned, but constitutional debility, neurasthenia and mental weakness may continue for months; such being the effect of protracted disease of a grave character, and of the exhausting effects of a tropical climate. All this emphasises the necessity for continued rest, prolonged absence from a hot climate, and careful avoidance of errors of diet, fatigue and over-excitement or variation of temperature.

Pathological Anatomy.—The chief lesions are those in the ileum, and occasionally in the upper part of the colon. The mucous membrane of the ileum is generally found in a catarrhal condition, especially marked at the lower end near the ileo-cæcal valve. The Peyer's patches are ulcerated in the direction in which they are arranged: the ulcers are often deep, with well-defined edges, and, extending to the muscular coat of the intestine, occasionally perforate it; in which case the evidences of peritonitis will be present. The solitary glands also are the seat of ulcerations. Limited ulceration may be found in the large intestine near the ileo-cæcal valve. In the earlier stages (during the first week) Peyer's patches are raised and swollen almost in a fungoid form. A similar condition is presented in a less degree by the solitary glands. This is the state of infiltration. In the second week ulceration takes place, and sloughing of the glandular tissues. In the third week, when these sloughs have separated, ragged, more or less deep, ulcerations are found, which, even after convalescence has set in, may remain unhealed for a considerable time. In favourable cases these ultimately cicatrise, but do not appear to contract the intestine. In mild cases, where recovery takes place early, it is possible that little or no ulceration has occurred, and that resolution has taken place. The lesions may extend over a considerable portion of the ileum, but they are generally confined to its lower end, and where the Peyerian patches predominate.

The mesenteric glands are enlarged and softened, sometimes caseous.

In some cases small ulcerations scattered over the surface of the ileum represent the intestinal lesions.

The liver is not unfrequently somewhat enlarged, showing traces of degeneration in the hepatic cells.

The spleen is generally, perhaps always, enlarged, softened, and of a darker colour than usual.

Commencing granular degeneration in the cells of the kidneys may be found; more extensive lesions are probably the results of other disease.

The larynx is sometimes found ulcerated; the lungs may be hypostatically congested, or the seat of pneumonia.

The heart is flabby and softened, showing signs of commencing degeneration of the fibres, the result of the fever process and the continued high temperature, and in this the muscular system generally is concerned.

Other pathological conditions may exist, but the lesions described are those that specially belong to this form of fever.

Treatment.—The treatment of ordinary enteric fever is much the same in India as elsewhere. It is of great importance that the patient should be placed in a well-ventilated room, and that in the hot weather the heat should be tempered by punkah, thermantidote, or other artificial means of cooling; the temperature should be kept as equable as possible.

But little medicine is required. Attention must be directed to the reduction of temperature, the calming of vascular excitement, the controlling of diarrhœa if present, perfect cleanliness, and the due administration of appropriate nutriment. The bed and body clothing should be so arranged that they can, if necessary, be frequently and easily changed. In no cases is good nursing more essential than in these. The bed should be of such a size as to enable the patient to be easily handled; and it is as well to have another one in order that the patient may be moved from one to the other as occasion requires. He should be protected from mosquitoes and other insects either by a deeply-fringed punkah or by a mosquito curtain. A supply of ice should be kept at hand, and if the cold bath treatment be adopted, mechanical means for lifting the patient in and out of the bath. Arrangements should be made for supplying fresh cow's milk day and night. Beef tea and extracts of meat should also be available.

The dietetic management has been already described in the articles on Dietetics and Sick Feeding, and on Enteric Fever [vol. i.]

Cold bathing, as described in the article on Hydrotherapeutics, has a great effect in diminishing fever; but this frequent transition from bed to bath, including the difficulty of having sufficient attendants to effect this properly, may produce so much fatigue and exhaustion as to counteract the benefit otherwise obtained. Cold packing, or the douche, or ice, a tray of which may be suspended over the patient under a cradle, is also useful in reducing temperature.

At the outset in vigorous persons, when the temperature is rising and showing an increased tendency to rise, I advocate the use of quinine in 3 to 5 gr. doses given every three to four hours—on account of its antipyretic properties—until an impression is made upon the temperature. When the fever is of a malarial origin, or is combined with malaria, the doses may be increased, for, in the latter case especially, the antiperiodic and parasiticide properties of the drug are also likely to be of service. In other respects Indian practice differs in no important respect from the European. Indeed, a case of typhoid fever pursuing an ordinary course, whether at home or abroad, requires very little interference on the part of the physician, beyond the prompt relief of any complications that may arise; and in a large number of cases they do not arise. The question of stimulants is perhaps the most critical one. In simple cases they are unnecessary; but high temperature, above 103° or 104°, dry and brown tongue, delirium, and signs of cardiac failure, indicate their necessity. In this case reduction of temperature, steadying of the feeble pulse, improvement in the first sound of the heart, which may have become weak, and in the respiration, moistening of the tongue, and a general mitigation of the hebetude and stupor of the countenance, will all indicate the benefit that is being derived from them. The pulse, the temperature, the tongue, the heart sounds, therefore, will be the guide for their administration and disuse. From 8 oz. to 12 oz. or more of brandy or whisky may be necessary in the twenty-four hours, or double the quantity of port wine; especially in persons who have been addicted to the free use of stimulants.

No case of typhoid should be despaired of. People recover even from the very worst conditions, whilst, on the other hand, cases apparently the most trivial may manifest severe and dangerous symptoms.

Convalescence is protracted, and must be guided with watchful care. Errors in diet are especially to be guarded against. The lightest and simplest food, though sufficient for nourishment, should be continued for some weeks. New articles of diet, however simple, should be gradually and tentatively introduced, nor should the patient give way to his appetite for a considerable time after he feels it has returned.

Neglect of these precautions has been over and over again followed by dangerous relapses. As soon as the patient is able to travel with safety, he should be moved to a temperate climate, where the precautions must not be relaxed for some months. Errors of diet, chill and fatigue should all be carefully avoided. Return to India should not be permitted until health and strength have not only been restored but established for some time.

It is hardly necessary to add that a careful record should be kept throughout of food and stimulants administered, of the temperature curve, of the pulse, and the excretions. In no form of disease is the constant attention of a competent nurse more important than in these fevers.

Prophylaxis.—Whatever the primary cause of enteric fever, which according to prevailing opinion is an acute infective disease due to a specific bacillus, there seems to be little if any doubt among the great majority of observers that the contagion exists in the alvine discharges of the sufferers. The necessity, therefore, is obvious for so disposing of those dejecta as to render it impossible for the poison to find its way into the human body through the medium either of water or of air.

Whilst fully recognising the importance of recent bacteriological research, yet knowing how rapidly it is revealing new and modified forms of these micro-organisms,—considering, moreover, that uncertainty exists with reference to their life history and morphological development, and that the most strenuous advocates of an exclusively bacillary origin are unable to declare this to be proved,—it is expedient, at least, to maintain some reserve in accepting the view that this micro-organism is the sole effective cause of enteric fever. Neither denying nor affirming the view that it is the sole cause in temperate climates, I agree with others who hold that the origin of fever with enteric symptoms in India must be sought for also in a wider and more general etiology, that is, in those conditions to which Murchison (41) gave the name of pythogenic, the formation of ptomaines or toxic agents autogenetically produced, the miasmata of decaying organic matter, the various meteorological and telluric conditions comprehended under the term climatic influences, and in malaria itself. The fact that enteric fever occurs largely in some of the hill stations of India where malaria can hardly be supposed to exist, and where there is no special reason for assigning it to a specific contamination, would seem to indicate a spontaneous origin of the contagium from pythogenic causes as suggested by Murchison—at all events where it has not been taken up from the plains.

But whatever view may be held on this subject, prophylactic measures must be based upon ascertained facts, and, fortunately, in the present aspect of the question, experience has taught that sufficiency and purity of water, milk, and all other potable fluids, the absence of decaying organic matter, of putrid emanations from sewers or cesspools or of soil infiltrated with fæcal matter, and provision for sufficient ventilation and cubic space are the surest prophylactic measures that can be taken against the origin and propagation of enteric fever. Medical officers of experience who have studied this disease, whether in its endemic, epidemic or sporadic form in India, and who fully recognise the great importance of bacteria as causal agents, are yet constrained to admit that the bacterial theory does not in India cover all the facts as regards fever with enteric lesions.

Nevertheless on all grounds it is right that the dejecta should be destroyed or disinfected, burnt if possible, or, when this is not possible, rendered innocuous by being mixed with a solution of ½ oz. of corrosive sublimate, 1 oz. hydrochloric acid, to 3 gallons of water; or if other means of disposing of it do not exist, by burying it two or three feet deep in soil, as far as possible from human habitations or the water-supply. Similar precautions should extend to the clothes; and all articles that may be soiled by the discharges should be completely disinfected by heat or other efficient measures; small things of little value should be burnt.

Sewers are not common in India, except in some large cities; but wherever found they should be sufficiently trapped and leakage prevented. Cesspools should be done away with as much as possible, or they as well as surface drains should be kept thoroughly clean. The greatest care must be taken to preserve the purity of the drinking-water; that from tanks should be prohibited; mussacks, earthen jars, filters, or other utensils in which it may be held or stored, should be constantly inspected and thoroughly purified. The masonry of wells or reservoirs should be kept in perfect order and thoroughly cemented; it should be so raised above the ground that surface drainage and percolation into them would be impossible, and all organic refuse prevented from finding access to the water.

Milk has been frequently charged with being the vehicle by which the poison is conveyed in India, therefore it cannot be too closely inspected and its purity established; but it is interesting to know that in some instances where outbreaks have been ascribed to it, women and children who have drunk largely from the same sources have suffered less than men.

As it is incontrovertibly shown that young people under 25 suffer very much more than at a later period of life from the disease, it is a fitting subject for consideration whether it might not be better to send out soldiers and young people above that age—say 25 to 30, instead of 20 to 24.

With regard to the results of malaria and insanitary influences, reference may be made to the remarks on the subject of prophylaxis under the heading "Malarial fever."

The foregoing sketch of this group of fevers by no means exhausts the subject, for of these there is still much to learn besides of other fevers that are not included in this article.

While expressing my admiration of the scientific acumen and zeal with which bacteriological researches are being pursued, and acknowledging their supreme importance, I would venture to deprecate hasty generalisation and the assumption that micro-organisms are always the sole cause of this or other forms of disease. Indian experience teaches that other agencies, which have been frequently referred to in the above paper, have a share in the etiology as in the development and modification of Indian fevers.

> Filosofia, mi disse, a chi la intende,
> Nota non pure in una sola parte,
> Come natura lo suo corso prende.
> *Inferno*, canto xi.

JOSEPH FAYRER.

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J. F.

TYPHUS FEVER

SYNONYMS.—Germ. *Fleckfieber*, *Flecktyphus*; French, *Typhus exanthématique*; Ital. *Dermo-tifo*, *Typho esantematico*; Spanish, *Tifus*, "*El Tabardillo*" or "*Tabardiglio*" (from *tabardo*, a cloak of dark cloth worn by the peasantry in Spain); Dutch, *Vlekkoorts*, *Kwaadardigekoorts* (*i.e.* malignant fever); Swedish, *Fläcktyfus*; Norwegian or Danish, *Nervefeber*, *Exantematisk Tyfus.*

TYPHUS FEVER is an acute, specific, highly infectious disease which prevails in epidemics; particularly in times of destitution and in the presence of overcrowding with deficient ventilation. It is characterised by a sudden onset with marked nervous symptoms, namely, rheumatoid pains, rigors and headache. A peculiar measly or rubeoloid rash appears most commonly on the fifth day of the disease. This consists of slightly elevated spots of varying size and shape, at first deleble on pressure (*maculæ*), afterwards persistent and darker (*petechiæ*). This rash is commonly present, except in young children; but its presence must not be considered essential to the diagnosis of typhus. It results rather from dissolution of the blood or from bacterial thrombosis than from dermatitis. There is early and usually extreme prostration both of the nervous system (*ataxia*) and of the muscular system (*adynamia*).

In the second week of the fever delirium is commonly present, sometimes of an acute and noisy type (delirium ferox), accompanied, it may be, by much muscular agitation and restlessness (delirium tremens), but oftener of a low, listless, muttering kind with somnolence (typhomania of Galen). In this case there is a tendency to stupor or coma.

The fever terminates by a crisis, which generally happens on or about the fourteenth day, and takes the form of a deep and prolonged sleep, a diuresis with deposits of urates in the urine, a moderate diarrhœa, or slight diaphoresis with quickly reviving intelligence. Profuse clammy sweating at the time of crisis is universally and justly regarded as a most unfavourable sign. Its occurrence is associated with extreme nervous prostration; a condition which constitutes the so-called "typhoid" or "ataxic" state.

During the fever the mucous membranes are generally the seat of a passive catarrh; and as the bronchial tract is the most affected, the disease used to be called *catarrhal typhus* in Ireland, while Rokitansky named it *broncho-typhus* or *pneumotyphus.*

In fatal cases no specific lesion is found beyond a widespread congestion and "dissolution of the blood," as well as a granular degeneration and cloudy swelling of the tissues of the nerves, muscles, and great viscera. None of these lesions, however, is of constant occurrence or peculiar to typhus.

The Greek term τῦφος (*smoke, mist, fog*) was employed by Hippocrates to define a confused state of the intellect, with a tendency to stupor (*stupor attonitus*); and in this sense it is aptly applied to typhus fever with its slow cerebration and drowsy stupor. Boissier de Sauvages first (in 1760) called this fever "typhus," and the name was adopted by Cullen of Edinburgh in 1769. Previous to the time of de Sauvages typhus was known as "Pestilential" or "Putrid Fever," or by some name suggested by the eruption, or expressive of the locality in which it appeared, as "Camp," "Jail," "Hospital," or "Ship Fever" (Murchison).

Ætiology.—Typhus is mostly a disease of the temperate and cold zones, a result which is in some measure due to the mode of living adopted by people resident in cold climates. They congregate in badly-ventilated houses rather than live an open-air life. This fever has from time to time prevailed in all parts of Europe, but it has had its peculiar habitats in Great Britain and Ireland, and in Russia. In the United States and British North America it has prevailed epidemically at various times. It is hardly known in Australia, New Zealand, India, Africa, or in the tropical and subtropical parts of North and South America. The Irish race has been especially prone to the disease, probably from the habits and comparative poverty of that people. "The history of typhus," Hirsch observed, "is written in those dark pages of the world's story which tell of the grievous visitations of mankind by war, famine, and misery of every kind." He added, "The idea that overcrowding in filthy and unventilated rooms affords the essential condition for the development of typhus-foci and for the spread of the disease has been completely borne out by the experience of all times." Epidemics of typhus are yearly becoming more and more rare. The most recently recorded outbreak is one which occurred in Sheffield in 1890, and was described by Dr. Theodore Thomson, Inspector of the Local Government Board (England).

In all cases, practically, typhus arises from the reception into the system of a specific poison—the virus or contagium of the disease. Of the intimate nature of this poison we are still ignorant, although analogy points to some micro-organism or its products as the *causa causans* of the disease. Hlava (1891) and Lewaschew (1892) are among the most recent writers on the bacteriology of typhus. Nothing definite, however, has as yet resulted from their researches or those of other investigators.

The *materies morbi* is cast off in the breath, from the skin, possibly in the evacuations also. It is then conveyed through close air, or by fomites, and, inhaled or swallowed, finds its way into the blood of fresh victims. Actual contact with the sick is not essential for the transmission of typhus; yet the striking distance of typhus is not great. Unlike the contagia of small-pox and scarlatina, the poison of typhus does not cross open-air spaces; it is readily neutralised, probably by oxidation, on coming into contact with fresh air. It is quickly absorbed by articles of clothing, bedding, furniture, and beams of wood; particularly by dark-coloured rather than by light-coloured woollen articles of dress. Such carriers of infection are technically called "fomites" (Lat. *fomes, fomitis*, touch-wood, tinder). Typhus is non-inoculable, but eminently infectious or "catching." There is no evidence that it is communicable to the lower animals. One attack generally confers immunity from a second. The disease is most infectious or "catching" during the period of convalescence. Its poison is very volatile and lighter than atmospheric air. There is strong presumptive evidence that dry heat (96° C. = 204·8° F.) is a powerful disinfectant agent in the preventive treatment.

The doctrine of the *de novo* or spontaneous generation of typhus is opposed to all analogy, so far as the specific fevers are concerned; indeed it is beset with greater difficulties than those which it is designed to explain. The theory is unnecessary if we assume the microbic origin of this fever, and remember how great is the vitality of the "resting spores" of pathogenetic micro-organisms. It must, however, be admitted that now and again a case of typhus occurs in which it is impossible to trace the infection. A striking example of such a case is reported in the *Indian Medical Gazette* for August 1895, by Surgeon-Lt.-Colonel R. H. Quill, A.M.S., Mhow, India: the patient was a gunner in the Royal Artillery, with five years' Indian service, and three months' residence in the station (Deolali) where his illness occurred.

The *bacteriology* of typhus fever is still imperfect. Researches on the subject have been in progress since 1868, when E. Hallier, of Jena, announced his discovery of a typhus fungus (*Rhizoporus*). In 1883 Mott described actively motile dumb-bell cocci in the blood of typhus. In 1891 Hlava of Prague found in the blood in twenty out of thirty-three fatal cases of typhus a peculiar, well-defined bacterium, to which he gave the name of *Streptobacillus*, and which he regards as the cause of the fever. Lewaschew, in 1892, described organisms which he had found in the blood of the spleen or finger of typhus patients, and which he regarded as a cause of the disease. In fresh blood these organisms appear as small, round, highly-refractile, actively moving bodies, lying between the corpuscles. Sometimes the organism is oval in shape and flagellate, or it may appear as a thread slightly enlarged at one end. These are probably different forms of the same microbe. Lastly, Dubieff and Bruhl (1893) found in the blood and spleen a diplococcus, called by them *Diplococcus exanthematicus.*

An individual is rendered more susceptible to the influence of the primary exciting cause of typhus—that is, of the essential or specific poison, virus or contagium of the disease, whatever its nature may be—by certain accidental circumstances, themselves insufficient to generate the fever, to which the term "predisposing causes" is applied. The chief predisposing causes of typhus are, in the order of their ætiological importance, destitution and defective nutrition, overcrowding, bad ventilation. In addition to these, the prevalence of typhus is more or less favoured by the winter season, intemperance, recent residence in an infected locality, previous illnesses, bodily fatigue and pain, loss of sleep, mental anxiety, and depressing emotion such as sorrow, fear, disappointment and worry. In the presence of a group of these factors a small and hitherto inert dose of the fever-poison may kindle a serious attack of typhus in such a way as to suggest that the fever has arisen spontaneously or *de novo.*

Clinical Description.—In typhus fever there seems to be no fixed duration for the *period of incubation* or the latent stage. In a large number of cases it is about twelve days; it rarely, if ever, exceeds three weeks. In many instances (one-third or more) it is less than twelve days, and occasionally there is scarcely any latent period, the symptoms commencing almost at the instant of exposure to the poison. Frequently the patients are conscious of the moment at which the fever-poison enters the system. One or two days of slight indisposition, shown by lassitude, vertigo, slight headache and loss of appetite, may precede the actual onset of typhus, which is sudden. The earliest symptoms are referable to the nervous system; they are chilliness or slight rigors, languor, frontal headache, pains in the back and limbs, especially the thighs. Giddiness, noises in the ears (*tinnitus aurium*), and disturbed sleep or sleeplessness are commonly present. If sleep occur it is haunted by dreams, and the patient rambles in his sleep. A sense of complete exhaustion quickly overwhelms the sufferer, so that by the third day he is fain to take to his bed. In this, the *stage of invasion*, other symptoms are loss of appetite, constipation, sometimes nausea but without vomiting, coated tongue, quick pulse, flushed and dusky face. The expression at first betokens weariness, but soon becomes dull, heavy, and listless. Afterwards the aspect becomes vacant and bewildered, sometimes wild and defiant. The face is flushed, with a dusky, earthy or leaden hue. Such is the *facies typhosa.*

The *stage of nervous excitement*—also called the *eruptive stage*—follows. It commonly extends from the appearance of the rash on the fourth or fifth day until the commencement of somnolence or stupor. Its leading features are restlessness, wakefulness and delirium. During this stage headache gives place to raving, and the tongue grows dry and brown, while collections of sordes gather on the lips, teeth and gums. These consist of proliferated epithelium which has desquamated quickly, fragments of food, dried mucus, saliva and blood, with various micro-organisms. The resulting mixture becomes black from desiccation, and has a heavy, offensive smell. The presence of abundant deposits of sordes is so far a proof of a severe attack and of seriously impaired vital powers.

The rash, or exanthem, of typhus in its earlier stage often closely resembles that of measles; hence the terms "morbilliform," "rubeoloid," and "measly" are often applied to it. It consists of spots or maculæ of very irregular size and outline, and of a dirty pink or florid colour. These appear first near the armpits and on the wrists, then on the sides of the abdomen, afterwards on the chest, back, shoulders, thighs and arms. They are rarely seen on the face and neck. At first, and particularly in mild cases, these maculæ are slightly elevated and deleble on pressure, like the velvety papules of measles. They have, however, no defined margin, but merge insensibly into the colour of the surrounding skin. Beneath the cuticle another crop of maculæ often appears, causing a characteristic marbling or mottling of the skin, hence the expression "subcuticular mottling." The superficial spots and the deeper mottling together constitute an eruption, to which Sir William Jenne. first gave the name of the "mulberry rash" of typhus.

Towards the *close of the first week* headache commonly gives place to delirium or raving, which may last up to the time of crisis. The delirium is sometimes acute and noisy like mania (*delirium ferox*); sometimes more like that of excessive alcoholism, being accompanied by muscular agitation, trembling and talkativeness (*delirium tremens*); and sometimes of a low muttering kind (the *typhomania* of Galen). The nervous excitement is most marked towards evening and at night. Prostration takes its place in the morning.

About the tenth day the *stage of nervous prostration* succeeds that of nervous excitement. It is also called the "putrid," "malignant," or "typhoid" ("ataxic") stage, or the "later eruptive stage." This is a most critical period in typhus, and when its ominous symptoms are well marked the patient's life hangs trembling in the balance. Extreme nervous prostration (ataxia), muscular and cardiac weakness (adynamia), defective cerebration, low muttering delirium, stupor and unconsciousness deepening into coma, are the phenomena which show themselves in "ataxo-adynamic typhus," as this grave form of the fever is called. The patient lies on his back and sinks down in the bed (prostrate dorsal decubitus), he moans and mumbles to himself incoherently, is indifferent to all that goes on around him, looks stupid and unconscious, with injected ferret-like eyes, contracted pupils (the "pinhole pupil" of Graves), teeth coated with sordes, and dry, brown-crusted, shrivelled tongue—the "parrot-tongue" of typhus. Deafness is also a common symptom. Various involuntary movements take place, such as tremors, twitchings of the muscles (*subsultus tendinum*), spasmodic twitchings of the face, perhaps choreic convulsions, or more usually picking at or fumbling with the bedclothes—the so-called "floccitatio" or "carphology." Obstinate hiccough (*singultus*) often accompanies these movements, and is a very grave sign. Not uncommonly, also, involuntary evacuations take place from paresis of the sphincters of the rectum and bladder. The pulse is rapid (112-145), small and soft; the respirations are shallow, frequent (40-48), blowing and noisy—the "cerebral breathing" of Sir Dominic Corrigan.

Simultaneously with the onset of these unfavourable symptoms the eruption changes in character, becoming darker in colour and quite indelible on pressure. The spots are no longer elevated, and in the centres of many of them dark purple or bluish points appear,—the true *petechiæ*, which Murchison defines as consisting of an infiltration of dissolved hæmatin into the tissue of the cutis. The peculiarity of typhus, so far as the rash is concerned, is that the eruption, in its earlier stage, is a true exanthem due to hyperæmia, or, it may be, congestion of the cutaneous capillaries, the outcome of "ataxic angio-neurosis" (Unna, 19), whereas in its later stages an escape of blood-pigment into the cutis from the broken-up red blood corpuscles is substituted for this hyperæmia or congestion. The maculæ are, in a word, converted into petechiæ. Unna, however, maintains (20) that the doctrine of "blood dissolution" in infective diseases is obsolete; and with Klebs he connects the cutaneous hæmorrhages of these diseases with blocking of the vessels of the skin by bacteria. The infective forms of purpura are, according to him, most simply explained in this way; and he thinks that the theory of bacterial coagulation thrombi will probably in future play an important role. Applying this view to typhus, the petechiæ would be the result of a diapedesis depending in its turn on clotting of plasma and consecutive stagnation round bacterial emboli.

The earlier and more marked the "typhoid state" just described, the more severe the case. The older writers spoke of it as the "putrid" or "malignant state." It is, however, by no means peculiar to typhus, for it may supervene in small-pox or scarlatina, and indeed in any idiopathic fever, blood-poisoning, or local inflammation.

In such a dire strait the patient may lie for many hours, or several days, until the stupor passes into profound and fatal coma, the "coma-vigil" of Sir William Jenner. In this most deadly trance the sufferer lies with his eyes wide open, with a vacant gaze and widely-dilated pupils insensible to light, his lips parted, his face pallid and devoid of all expression, the pulse rapid and feeble or imperceptible, the breathing hardly to be detected, the skin cold and clammy or bathed in sweat. Although awake the patient is insensible, and surely dies. In other cases sudden engorgement of the lungs, with asphyxia, supervenes, or the heart fails, with coldness and lividity of surface, and profuse sweating; death ensues from syncope and coma combined. Or again some fatal complication may seize and carry off its victim—a widespread bronchial effusion, it may be; or the so-called hypostatic congestion of the lungs, or laryngitis, or inflammation, or degeneration of the kidneys, with uræmic convulsions, or gangrene in its varied forms of bed-sore, spontaneous gangrene from arterial thrombosis, and noma or cancrum oris (gangrenous stomatitis).

Happily, such is not always or even frequently the end of an attack of typhus. Usually, on or about the fourteenth day there is a more or less sudden and rapid improvement in the patient's condition, and the *stage of defervescence or crisis* ensues. At the time named the patient falls into a quiet and prolonged sleep, from which he awakes at first, it may be, bewildered and confused. Soon, however, he recognises those around him, and for the first time is conscious of his profound weakness. The pulse beats less quickly and the temperature falls, the tongue becomes moist and clean at the edges, the skin is moist or the bowels are relaxed, or the urine deposits lithates (urates) in abundance and is copiously secreted. In few acute diseases is crisis so marked as in typhus, and in uncomplicated cases the final defervescence, as recorded by the thermometer, is, to adopt Wunderlich's expressive phrase, usually "precipitous."

Once the temperature falls, restoration to health, or the *stage of convalescence*, goes on apace. The tongue cleans and is moist, the appetite may become ravenous (boulimia). Meanwhile the bodily powers improve day by day, so that in three or four weeks health and strength may be fully restored. Typhus but rarely lays the foundation of any permanent organic disease.

The **mean duration** of 500 uncomplicated cases ending in recovery was, according to Murchison, 13·43 days. That of 100 fatal cases was 14·6 days. When life was prolonged beyond twenty days the fatal result, in the same author's experience, was due to some complication. Dr. T. J. Maclagan investigated 581 uncomplicated cases which recovered in the Dundee Royal Infirmary, and found their mean duration to be 13·39 days—a value which is practically identical with Murchison's estimate.

Although the duration of typhus is thus about fourteen days, this fever may run a much shorter course. Malignant cases may terminate fatally on the second or third day, or even in a few hours. To such cases the name of **blasting typhus** or **typhus siderans** has been given. This terrible form of the disease is apt to prevail in times of war and destitution.

In ordinary times, however, cases of short duration—particularly among children—are not uncommon and are usually mild. Some of these patients show but little rash, but Murchison gives details of cases with eruption which terminated on the tenth or even as early as the eighth day.

Relapses are extremely rare in typhus. Not a single case of true relapse was ever seen by Sir William Jenner, A. P. Stewart, or Murchison. Out of 18,268 cases of typhus reported at the London Fever Hospital during twenty-three years, only one example of a true relapse was observed (by the late Sir George Buchanan); in several instances, however, a genuine has been preceded by an abortive attack. Buchanan's case was that of a nurse in the hospital, aged 42, who passed through a two-weeks' typhus. After a week's interval a relapse took place, with a recurrence of the rash, lasting upwards of a fortnight. A very similar case was recorded by W. Ebstein of Breslau in 1869. In this instance an interval of twenty-five days occurred between the two attacks.

Temperature.—No clinical description of typhus would be complete without an account of the behaviour of the temperature in the disease.

A sudden rise of the thermometer takes place at the outset, culminating in a fastigium or acme of 103° to 105° F., at some time between the evening of the fourth day and the seventh day or later. Except in severe cases, this is followed by a more or less pronounced remission of fever or *pseudo-crisis* early in the second week, generally between the seventh and tenth days. In mild cases this fall of temperature at the beginning of the second week may prove complete and final, a true crisis cutting the fever short ("Typhus levissimus," or "Mild typhus"). On the other hand, in grave cases a gradually rising temperature at this very period may culminate in a fatal hyperpyrexia (41°-43° C.) (105·8°-109·4° F.)

In many instances the pseudo-crisis at the beginning of the second week is succeeded by a second fastigium on or after the eleventh day. In favourable cases this does not attain the height of the initial fastigium in the first week. This second rise of temperature may be absent, the thermometer gradually falling through the second week until the fourteenth day, when it rapidly sinks to or below normal.

In a majority of cases defervescence is sudden. It may be preceded by a final evening exacerbation on the twelfth or thirteenth day,—a "critical perturbation," as Wunderlich called it. The descent of the temperature is then rapid, even precipitous, falling 3° to 5° F. or more in a single night, afterwards it rises some 2° in the evening, and finally reaches the normal point for the first time next morning. Such is the crisis of typhus. In its suddenness and completeness it closely resembles the abrupt defervescence in both measles and acute pneumonia (pneumonic fever), except that it occurs at the end of the second instead of the first week of the fever, as in the latter diseases.

Severe cases, with cerebral symptoms (ataxic typhus), show a continuously high range of the thermometer without any remission about the seventh day—indeed, the thermometer continues to rise through the second week. This is especially so when some complication is threatening, a state of things which may postpone defervescence indefinitely, or usher in a fatal excessive fever or hyperpyrexia.

On the other hand, in adynamic cases, with heart failure and pulmonary obstruction, the range of temperature may be moderate—not exceeding 103°—or irregular with "spiking" readings; or the fever may be continuous without morning remissions; or a fall of temperature may be observed with a rise of pulse-rate without any improvement in the general symptoms.

Fatal cases are usually accompanied by high readings of the thermometer from the outset, yet even in these cases it is not so much the intensity as the continuance of the fever which determines the mortal result. Just before death and in the death-agony a supreme rise of the thermometer is a constant and ominous phenomenon.

Afebrile typhus has occasionally been observed. Combeville (4) reported a case in which the temperature rose to 104° F. on the third day, then fell, and on the morning of the sixth day reached 92·6° in the rectum. The patient died next day with a temperature of 97·8°. A second patient had a temperature of about 100·4° only at the beginning of his illness. The curve then sank to between 96·8° and 98·6°, remained so until the ninth day, when a descent to 91·8° took place. Then again a rise to 96·8°; death with a reading of 95·9°.

A poisonous *odour* hangs about the person and especially the skin and breath of the typhus patient after the first week. It is highly infectious. With Murchison we may speak of it as a smell *sui generis*, though Gerhard aptly described it as "pungent, ammoniacal, and offensive." It most resembles that of the air in a low, damp and overcrowded dormitory after some hours of closure. This typhus odour is strongest in heavy, damp weather, and where ventilation is deficient. Sudamina, or sweat vesicles, local eruptions of herpes, purpuric spots and vibices are accidental manifestations (epiphenomena) on the skin in typhus. In convalescence desquamation takes place in fine branny scales (furfuraceous), and the hair usually falls off, although not to so great an extent as in small-pox. Interference with the nutrition of the skin and its appendages is shown by the frequent occurrence of a white band and a furrow at the lunula of the nails, four to six weeks after the commencement of the fever. These markings gradually advance to the tip of the nails.

Daily examination of the pulse, heart, and lungs should never be omitted in typhus. The circulation especially is much disturbed. The pulse is at first full, but soft and compressible, and moderately quickened (108-120 beats a minute); or it may be abnormally slow, down to 48, 40, and even 30 beats—often a sign of debility. When the patient sits up his pulse becomes quicker and less full; in the second week often dicrotous or undulatory. This is an indication of very low arterial blood-pressure; and a practical bearing of the observation is that the typhus patient should never be allowed to assume a sitting, much less a standing, posture.

The condition of *the heart* is profoundly altered in this fever. Weakening of the heart generally begins about the fourth or fifth day, and passes off after the tenth day in cases which are about to do well. The muscular tissue of the organ is softened and friable. All modern pathologists agree in attributing this change to cloudy swelling and granular fatty degeneration. Those who maintain that the change is inflammatory, speak of the disease as an "acute parenchymatous myocarditis," or "an infective myocarditis." Those who regard the condition as merely degenerative give to it the names of "acute parenchymatous degeneration," "albuminous degeneration," or "febrile softening of the heart." In it the heart is sometimes perceptibly dilated; the myocardium is of a dirty grayish red or grayish yellow colour, with occasional extravasations; its consistence is soft; its substance is lax, flabby and friable. Thrombi may be found in the ventricles. Microscopically the muscular fibres are swollen, their striation is more or less lost and replaced by granules (albuminous) and fatty molecules; occasionally they undergo waxy degeneration (Zenker). Along with these evidences of degeneration there are found certain appearances which suggest regeneration—a condition which certainly is established in favourable cases of typhus.

This acute parenchymatous change may be the result of the specific action of the fever poison, of the accompanying pyrexia, or of both, on the protoplasm (Mitchell Bruce). As regards the symptoms, cardiac failure is the chief evidence of this morbid condition of the myocardium. We are indebted to Dr. Stokes for a full clinical account of this febrile weakening of the heart. According to him the first objective symptom is a diminished cardiac impulse, even when the patient lies partly on the left side, in which position the apex of the heart comes into contact with the chest wall. The impulse, in the next degree, fails altogether, while the first sound becomes fainter or less loud. Occasionally a temporary bellows murmur accompanies this sound. These signs are most apparent towards the left, because the left ventricle is most affected. In the third stage of the lesion the first sound disappears, the heart being heard to beat with only one, and that the second sound, which may be actually accentuated from increased pressure in the pulmonary artery, or appear accentuated by contrast. In a yet more advanced stage of cardiac weakness both sounds are equally diminished in loudness and become equidistant, while the heart beats with great rapidity (tachycardia). The pulse-rate is now from 140 to 160 beats per minute. To this state the term "fœtal heart" has been applied, because in its weakness and from its quickness at the expense of the long pause it resembles the heart-beat of the fœtus in utero. This condition indicates great debility. The last stage of all is silence of the heart, a sign of impending dissolution, a condition which, as Stokes observes, is almost always fatal.

In making a physical examination of the heart allowance must be made for the muffling of the sounds under the influence of a very muscular or a very flat chest wall, or in the presence of loud bronchial râles and rhonchi.

Should the patient recover, the physical signs alter in the inverse order. Coincidently with the return of the first sound the pulse should fall in rate, otherwise the prognosis is bad. After the fever the pulse often falls much below the normal rate—even as low as thirty beats in the minute. It then slowly recovers itself.

In typhus, where there is no pulmonary complication of account, and where the nervous symptoms are not pronounced, the normal ratio of the respiration to the pulse—1 to 4—is maintained. Thus a pulse of 120 beats per minute would mean thirty respirations. In grave cases, however, certain *abnormal modes of respiration* may arise from cerebral disturbances, independently of any pulmonary disease. In such cases the breathing is hurried, sighing, irregular, spasmodic or jerking. There is a *besoin de respirer*, what the Germans call *Lufthunger*. This irregularity of breathing, independent of any pectoral affection, Graves called "cerebral respiration." In other cases the breathing is irregular, blowing or hissing, while the mouth is kept closed, the cheeks puff out, and the nostrils dilate with each expiration; this is the "nervous or cerebral respiration" of Sir Dominic Corrigan. A third variety is the rising and falling breathing, to which the name of "Cheyne-Stokes' respiration" has been given. This peculiar form of dyspnœa consists in a series of inspirations increasing in rapidity and depth to a maximum, and then declining in force and length until a state of apparent apnœa is established. When this has lasted for some moments—occasionally so long as to suggest that death has actually occurred—a low inspiration, followed by others more and more decided, marks the commencement of a new ascending and descending series of inspirations.

Hypostatic congestion very often takes place in the most dependent parts of the lungs. Its causes are—impaired innervation (paresis of the pneumogastric nerves), impaired nutrition of the blood-vessels, and lessened heart power. The occurrence of this serious complication is favoured by the greatly impaired movement of the chest walls and the dorsal decubitus, in which the patient lies on the broad of his back. Physical examination of the chest day by day affords timeliest warning of the stealthy approach of this perilous condition, and should never be neglected in typhus. There may be neither cough nor expectoration, but the rapid laboured breathing with cyanosis due to defective aeration of the blood should draw the attention of the physician to the patient's danger from serous œdema of the lungs. The physical signs may be those of a widespread bronchial catarrh.

The breath of a typhus patient is offensive, heavy and pungent, often ammoniacal. Its smell has been likened to that of yeast. The absolute quantity of carbonic dioxide in the lungs is increased, but the proportion of this gas in the expired air is considerably below the normal amount. This anomalous result, arrived at by Dr. A. Malcolm of Belfast in 1843, is explained by Vierordt's observation that, even in health, the proportion of carbonic acid in the expired air diminishes as the respirations become quicker.

Bronchial catarrh may usher in, accompany, or succeed an attack of typhus. It is a dangerous complication, particularly in winter—first, because it is almost certain to be associated with more or less hypostatic consolidation in the lungs; secondly, because the bronchial secretion is likely to accumulate in the tubes and asphyxiate the patient in consequence of his inability to cough, coupled with the impaired nutrition and paralysis of the muscular fibres of the bronchi. Pneumonia is a rare complication or sequel of typhus. It may be distinguished from hypostatic congestion (with which, however, it is sometimes associated) by the fact that the dulness is unilateral, and by the presence of tubular breathing and rusty sputa. Pulmonary gangrene is a rare but fatal complication, which is apt to occur in very destitute patients. It may be of embolic origin, secondary to extensive bed-sores over the sacrum, as in cases observed by Murchison. Pleurisy, with purulent effusion, is a rare and may be a latent complication. Tuberculosis of the lung also is an infrequent sequel of typhus, although it is by no means uncommon after enteric fever.

In this connection mention should be made of laryngitis as a rare but dangerous complication of typhus. In Germany its occurrence led Rokitansky to give to this variety the name of Laryngo-typhus. It may be croupal in character, or show itself as acute œdema of the glottis. When the inflammation involves the cartilages it is called "perichondritis laryngea typhosa."

As regards *the urinary system*, the renal secretion is much diminished at first, when it is acid, dark-coloured from typhous dissolution of the blood, and of high density (1024-1036). Urea is increased in quantity at the outset, but afterwards falls below normal, on account of low diet and imperfect elimination. Albuminuria is often present, but this does not necessarily imply renal disease; for in excessive blood-changes such as occur in bad typhus, the blood serum may find its way into the urine. Uric acid is usually increased, and both Frerichs and Murchison have detected leucin ($C_6H_{13}NO_2$) and tyrosin ($C_9H_{11}NO_3$), two products of the disintegration of albumin or fibrin, in the urine of typhus. Chlorides gradually lessen in amount from the first. Towards the close of the fever there may be diuresis—a recognised mode of crisis, with a copious precipitation of urates. General convulsions are most dangerous in typhus. They occur in about one per cent of the cases, and with rare exceptions are of uræmic origin. In most of these cases there is albuminuria, with scanty or suppressed secretion. Kidney disease is often present, or there may be a history of intemperance. Uræmic convulsions do not usually appear before the middle or end of the second week. Murchison took notes of sixty-nine cases of convulsions in typhus. Of these, sixty-one were fatal, and only eight recovered. Occasionally simple retention of urine determines an attack of epileptoid convulsions, in which case judicious treatment may afford immediate relief. The catheter should be passed, as recommended by Dr. Stokes, after a few whiffs of chloroform have been cautiously given, if this be necessary.

Convulsions are commonly preceded by drowsiness or delirium. Allusion has more than once been made in this article to the important part played by *the nervous system* in the symptomatology of typhus. Frontal headache is an early and constant symptom. It is a dull, aching, heavy pain—rarely acute, darting, stabbing, throbbing or bursting. It is the most characteristic nervous symptom during the first week, when, however, vertigo and rheumatoid pains in the back and limbs may also be troublesome. Mental confusion or actual delirium takes the place of headache towards the close of the first week; hence typhus has often been called "brain fever." The mind becomes blunted and dull, memory lapses, and cerebration is slow and defective; in this state the term "typhus" becomes singularly appropriate. The delirium varies in character, as has been already stated. Of the three types—typhomania, delirium tremens, delirium ferox—the first is the most common, the last is the least common. "The mental state of the delirious typhus patient," wrote Murchison, "is peculiar, and well worthy the study of the metaphysician. As a rule the memory is first and most affected; judgment and power of connected reasoning often remain after the memory has entirely gone. The mind may labour under the strangest delusions, and often it appears to revolve obstinately around some fixed idea. The patients rave about objects which have greatly engrossed their attention, either immediately preceding the attack, or years before, and which are now jumbled with persons, scenes, and events with which they have had no connection."

Wakefulness is a common symptom in early typhus. It is apt to be followed by extreme nervous agitation and prostration, or by somnolence, deepening into complete coma and terminating in death.

Various muscular paralyses are observed in the course of the fever. Paralysis of the neck of the bladder, coming on about the tenth or eleventh day, leads to involuntary dribbling of urine; paralysis of the sphincter ani to incontinence of fæces. The coats of the bladder may lose their power from over-distension, causing retention of urine, and incontinence and retention may even coexist. Meteorism is due to paresis—that is, partial paralysis—of the walls of the intestines. The orbiculares palpebrarum may lose their power, so that the patient cannot close his eyelids, and keratitis and even sloughing of the cornea are induced from exposure. Aphonia, inability to protrude the tongue and dysphagia are other examples of typhous paralyses—the last-named being the worst of all, and usually the forerunner of death.

Muscular agitation indicates great prostration and is of grave import. It is observed in patients who are old and infirm, or intemperate, or brain-workers. Its forms are: tremulousness of the hands, tongue, or whole body; rapid oscillatory movements of the eyeballs (nystagmus); choreiform movements of the extremities; choreic convulsions; twitching of the tendons of the wrist (subsultus tendinum) and of the facial muscles; picking at or fumbling with the bed-clothes (floccitatio or carphology); and obstinate hiccough (singultus).

Muscular rigidity is much rarer than muscular agitation, although equally unfavourable; the fingers may be clenched, or the forearms flexed. There may be tonic spasms of certain muscles, or even trismus or strabismus. Well-marked opisthotonos, with the head bent back and the limbs rigid, was once observed by Murchison and once by Perry—both cases proved fatal. Of general convulsions I have already spoken.

The *organs of special sense* suffer in proportion to the severity of the fever. The suffused conjunctivæ and contracted pupils—"pinhole pupils" of Graves—constitute "the ferret eyes" of typhus. In coma the pupils dilate and become insensible to light, with squinting. Inequality of the pupils has frequently been observed by Cayley, who regards the phenomenon as without prognostic significance. Photophobia is sometimes noticed. Tinnitus aurium and noises in the head are often present at the beginning and close of the fever. Deafness is commonly observed; if bilateral, it is probably part of the general anæsthesia of the fever, or it may be due to typhous softening of the intrinsic muscles of the ear (Stokes), or otitis may cause it. Intolerance of sound is a distinctly bad sign. The senses of smell and taste are often blunted or obliterated. Epistaxis, or nose-bleeding, is very rare in typhus.

The sensibility of the skin is usually lessened (hypæsthesia), impaired (paræsthesia), or entirely lost (anæsthesia); hyperæsthesia is occasionally observed. So far no instances have been recorded in which typhus has been followed by that linear atrophy of the skin, with or without hyperæsthesia of adjacent parts, which is a rare sequel of enteric fever, and which has been described by Sir Dyce Duckworth and Dr. S. Wilks of London, Dr. Shepherd of Montreal, Dr. J. R. Bradshaw of Liverpool, and several continental observers.

The chief determining causes of **the complications** which modify the course of typhus more or less unfavourably are—(i.) The weakened state of the heart; (ii.) the impure state of the blood; (iii.) constitutional peculiarities and family idiosyncrasies; and (iv.) the so-called "epidemic constitution" at a given time or place—that is, the special characters of the prevailing epidemic.

The complications which affect the respiratory organs are—(i.) *Laryngitis*, infrequent but dangerous, croupal in character, or showing itself as acute œdema of the glottis, and giving to this fever the name of laryngotyphus (Rokitansky); (ii.) *Bronchitis*, a very common and dangerous complication or sequel; hence the names "Catarrhal typhus" (Irish writers), "Bronchotyphus" and "Pneumotyphus" (Rokitansky); (iii.) *Hypostatic congestion* of the lungs, already described; (iv.) True *pneumonia*, a rare complication, or rather sequel of typhus, generally unilateral and accompanied by rusty sputa and tubular breathing; (v.) *Gangrene of the lung*, a rare and fatal complication, apt to occur in the most destitute patients, and likely to be of embolic origin, secondary to extensive bed-sores over the sacrum (Murchison); (vi.) *Pleurisy*, rare and latent, but with purulent effusion from the outset; (vii.) *Tuberculosis* of the lungs, a rare sequel; and (viii.) *Hæmoptysis*, exceptional, and resulting either from tubercular deposits, pulmonary apoplexy, or from acute hæmatolysis (Murchison).

As to the blood and circulatory organs, typhus, like small-pox, may so devitalise and defibrinate the blood as to establish—(i.) an *acute hæmophilia*, the patients becoming "bleeders" from "typhous dissolution of the blood, or from bacterial thrombosis as already explained." Hence the formation of purpura spots and vibices, and the occurrence of epistaxis, hæmoptysis, hæmatemesis, melæna, menorrhagia, hæmaturia, and other hæmorrhages. (ii.) *Pyæmia*, with purulent deposits in the joints, is a rare and fatal complication at the time of crisis or later. It is signalised by repeated rigors, unstable spiking temperature ranges, extreme prostration, heart failure, jaundice and profuse sweating. (iii.) *Venous thrombosis*, an occasional sequel, causing phlegmasia alba dolens, or "white leg." This condition may also result from obstruction of the lymph channels or inflammation of the subcutaneous areolar tissue (diffuse cellulitis). (iv.) *Arterial thrombosis and embolism* are occasional but serious complications or sequels. They cause local gangrene, cancrum oris, osseous necrosis, abscess or gangrene of the lungs, and splenic infarctions. Lastly, in the heart itself (v.) an *acute granular disintegration of the muscular tissue* often takes place, constituting a dangerous lesion, especially in advancing life; but pericarditis and endocarditis are extremely rare.

Profound though the influence of the poison of typhus is upon the nervous system, yet tangible pathological changes and complications connected with that system are infrequent. The cerebral symptoms of this fever are usually, perhaps almost invariably, independent of inflammation of the brain or its membranes. Nevertheless, *meningitis*, although rare, is met with in typhus, of which disease also *temporary fatuity* and *mania* are infrequent and very sad sequels. Happily recovery generally follows at last, usually in two or three months. *Paralysis* is a rare sequel. It commonly assumes the form of hemiplegia, but may occur as paraplegia or as general paralysis (H. Kennedy). *Peripheral neuritis* may be the serious cause in some instances of the muscular pains, which sometimes occasion much distress in convalescence, and protract recovery. The physiological deep reflex called the "knee-jerk" or "patellar reflex" is sometimes exaggerated; and the pathological deep reflex known as "ankle-clonus" is sometimes found in the stage of convalescence.

Lesions of the digestive tract are not common in typhus. *Erysipelas of the pharynx* may cause dysphagia or œdema of the glottis, and so endanger life. *Hæmatemesis* and *intestinal hæmorrhage* are rare but fatal complications: they result in the graver cases of typhus from the liquefied state of the blood. *Diarrhœa* and *dysentery* are occasionally met with—the latter complication in camps and sieges. *Jaundice* is infrequent, but fatal: of fifteen instances observed by Murchison, the jaundice was due to consecutive congestion of the liver in three cases, to gastro-duodenal catarrh in one case, and to some abnormal state of the blood in the remaining eleven cases, of which nine proved fatal. *Peritonitis* is almost unknown as a complication of typhus: in two cases seen by Murchison the causes were, respectively, the bursting of a softened embolic infarct in the spleen and tuberculosis of the peritoneum.

In connection with the urinary organs *nephritis* is a dangerous complication, often inducing fatal uræmic convulsions. *Cystitis* may result during convalescence from retention of urine and over-distension. Either of these affections may be accompanied by hæmaturia, which may also arise from acute hæmatolysis.

The integuments and bones may suffer severely as in enteric fever. *Bed-sores* are favoured by impaired innervation, but arise directly from pressure, early neglect, and want of skilled nursing. *Spontaneous gangrene*, independently of pressure, is probably brought about by arterial thrombosis; it affects the toes and feet, the nose, penis, scrotum and female pudenda. It occurs in badly-fed patients, and is ushered in by severe shooting pains, numbness, coldness and lividity. *Gangrenous stomatitis* (noma, or cancrum oris) is a destructive and fatal variety of gangrene, which attacks the cheek, mouth, tongue, and face of delicate, badly-fed children towards the close of the fever. "*Hospital gangrene*" attacks wounds and abraded or ulcerated surfaces in persons under the influence of typhus. It is identical with or closely allied to acute sloughing phagedæna. *Inflammatory swellings* or *buboes* are not infrequent at or after crisis, especially in the parotid and submaxillary regions. To Murchison this fact suggested the kinship of typhus and oriental plague or bubonic fever. He went so far as to say that "typhus is probably the plague of (? in) modern times." These bubonic swellings may terminate in purulent infiltration and abscess, or recede without suppurating. In the former case especially they are a formidable complication.

Lastly, typhus fever may be complicated by the coexistence or close sequence of such other specific diseases as small-pox, scarlatina, diphtheria, erysipelas and enteric fever.

The following, among many other **varieties of this fever,** have been described:—(i.) Inflammatory typhus, characterised by much febrile reaction in the young and robust, and in patients of the upper class; (ii.) Nervous or ataxic typhus ("brain fever"), in which nervous symptoms predominate and the rash is copious, dark, and petechial; (iii.) Adynamic typhus, accompanied by great muscular and cardiac prostration, involuntary evacuations, and a tendency to collapse; (iv.) Ataxo-adynamic typhus —congestive typhus—by far the most common variety; (v.) Typhus siderans, or "blasting typhus," very acute and most fatal; (vi.) Typhus levissimus, or "mild typhus"; (vii.) Abortive typhus in the "*typhisation à petite dose*" of Jacquot, in which symptoms occur in persons exposed to infection without developing into actual typhus; (viii.) Catarrhal typhus, an Irish appellation for the disease, because it is so often complicated with bronchial catarrh. For this reason also Rokitansky devised the names "broncho-typhus" and "pneumotyphus."

Diagnosis.—The rash is pathognomonic. Before it appears we have grounds for a differential diagnosis in a history of exposure to the infection of typhus, and of such symptoms after exposure as rheumatoid pains, headache, and early prostration. It may be necessary to distinguish typhus from the following diseases or diseased conditions, or *vice versâ*:—

1. Spirillum fever (relapsing fever).—In forming an opinion regard should be paid to the nature of other cases of fever occurring in the same house or family. In spirillum fever there is no rash, while epistaxis, jaundice, vomiting, and cardiac murmur are common phenomena. The febrile attack terminates by a critical defervescence after five or seven

days. This is followed by a remission lasting seven or eight days, and by a relapse on or about the fourteenth day, lasting some three days. This fever prevails epidemically, for the most part during seasons of scarcity and famine. The spirillum is to be found by appropriate means.

2. Enteric or typhoid fever, in contrast to typhus, begins insidiously, is often accompanied by diarrhœa, lasts at least ten days longer (twenty-four compared with fourteen days), terminates by lysis, has an unchangeable eruption, if any, of circular, lenticular rose spots, which never become petechial, and which fade after death. This fever also is characterised in general by a clear complexion, bright eyes, dilated pupils, comparatively moderate prostration; tenderness of the abdomen, tympanites, *gargouillement*, or gurgling in the ileo-cæcal region; early epistaxis also is common, and the pathological changes are specific, being found chiefly in the last few inches of the ileum and about the ileo-cæcal valve as well as in the mesenteric glands and the spleen.

3. Tropical remittent fever (jungle fever) is a parasitic disease, caused by protozoa (Laveran) in the blood. It arises independently of overcrowding, prevails in tropical climates and in warm and rainy seasons. The spleen is much enlarged, and quinine often acts specifically. Petechiæ may no doubt be present, but the macular rash of typhus is wanting.

4. Purpura is non-contagious, and, as a rule, apyrexial. It is unaccompanied by cerebral symptoms, but is attended with hæmorrhages from the mucous membranes. The spots are larger than the petechiæ of typhus.

5. Measles presents a characteristic history and epidemic prevalence. It is further distinguished by its prodromal catarrhal symptoms, the brighter tint and greater abundance of its rash, the frequent presence of diarrhœa, and its early defervescence. Its victims are usually children, who enjoy a comparative immunity from typhus.

6. In inflammation of the brain (cerebritis or encephalitis) or its membranes (meningitis) there is early delirium with excruciating headache. The senses are morbidly acute. The pulse is bounding. There is no rash like that of typhus. In meningitis loud cries or screams (*cri cérébral*) occur, also strabismus, ptosis, opisthotonos and partial palsy. There is extreme intolerance of light (photophobia) and of sound. Nausea and vomiting are common. A sign of dubious value is the appearance of a red streak upon the skin after pressure by the finger-nail (*tache cérébrale*).

7. The delirium tremens of the drunkard sets in with sleeplessness and delirium, without shivering, headache, or pains in the limbs. The tongue is moist and coated with a creamy fur, the skin is damp and cool. There is no eruption, and the temperature is not high.

8. Asthenic or typhoid pneumonia is distinguished, at any rate after the first day or two, by the presence of physical signs in the lung and the absence of eruption.

9. Uræmia chiefly occurs in chronic interstitial nephritis in advanced life, especially in gouty subjects or persons suffering under chronic lead poisoning (plumbism), and the temperature is normal or subnormal. This

last circumstance Murchison calls "the grand point of distinction." Finally, although the "typhoid state" may be fully developed in uræmia, the typhus rash is, of course, wanting; other rashes, however, may occur in uræmia (11).

Prognosis.—The unfavourable signs in a given case of typhus are—1, A presentiment of death, often entertained by physicians when ill of typhus; 2, A soft and compressible pulse, in rate above 120 in an adult; 3, Absence of cardiac impulse, and lessened or silent first sound of the heart; 4, Hurried respirations, particularly if no pulmonary lesion exist to explain this symptom; 5, Sleeplessness and delirium; 6, Complete coma-vigil of Sir William Jenner; 7, The presence of the pinhole pupil of Graves; 8, Great prostration; 9, Convulsions; 10, Muscular tremors and hiccough; 11, Relaxation of the sphincters before the tenth day; 12, Tympanites or meteorism; 13, Lividity of the face and surface generally; 14, Abundance and darkness of the rash; 15, Persistent high temperature; 16, Profuse sweating after the tenth or twelfth day; 17, The presence of any serious complication.

When death does take place it results from asthenia, with heart-failure; or from ataxia, nervous symptoms deepening into coma; or from some intercurrent complication or sequel.

Mortality.—The death-rate from typhus among the community at large probably does not exceed 10 per cent of those attacked. Hospital statistics show a higher rate. At the London Fever Hospital, in twenty-three years ending with 1870, the death-rate was 18·92 per cent. At Cork Street Fever Hospital, Dublin, in the last epidemic, that of the years 1880-82, the death-rate was 10·5 per cent. As in the case of other epidemic diseases, the mortality is greater immediately after the outbreak than in the later periods. During the twenty years ending March 31, 1891, 2895 cases of typhus were admitted to Cork Street Fever Hospital, Dublin. Of these, 363 proved fatal, the death-rate being 12·6 per cent, or nearly 1 in 8. Age influences the fatality of typhus in a most remarkable way. At the London Fever Hospital, among 18,138 cases, the mortality during the first five years of life was 6·69 per cent; in the second lustrum it fell to 3·59; between 10 and 15 it was only 2·28 per cent; between 15 and 20 it rose to 4·46. Of the patients above 30 years, 35·39 per cent died; above 40, 43·48; above 50, 53·87; above 60, 67·04; above 70, 79·00; and above 80, 100·00 per cent. And yet typhus is not invariably fatal in very advanced life, for in 1821 a man, said to have been aged 104 years, recovered from petechial typhus in the wards of Cork Street Hospital. Sex influences the mortality; men die in greater numbers than women. The intemperate, the sickly, the obese, or the very muscular, the hard-worked, whether bodily or mentally, but especially the latter, run the worst chance of all if attacked by typhus. Season affects the death-rate, which drops to a minimum as summer advances; but rises to a maximum in late winter and spring, which increase is probably due to concentration of the poison in closer rooms. Fatigue and privation, and particularly too late removal to hospital, are all prejudicial to the typhus patient. Pregnancy adds little to the danger of this fever, but suckling induces anæmia and increases the risk of death from exhaustion.

Pathological Lesions.—Cadaveric rigidity is of short duration, and putrefaction takes place rapidly. Emaciation is considerable, though much less than in typhoid fever. A widespread congestion (passive hyperæmia or stagnation of blood) is the most constant and noticeable post-mortem appearance. The petechiæ persist after death, and the blood in general is profoundly altered, being feebly coagulable, often staining the endocardium and the intima vasorum. Examined under the microscope rouleaux are absent, and the red blood corpuscles are crenated and misshapen. The muscular tissue of the heart is softened and friable. It is the seat of cloudy swelling and granular fatty degeneration. In the respiratory system there are traces of a widespread catarrhal inflammation of the air-passages and of hypostatic consolidations in the lungs. No evidence of acute inflammation of the brain or its membranes is forthcoming as a rule to account for the cerebral symptoms. The kidneys are not uncommonly hyperæmic and enlarged, while the tubes are stuffed with granular epithelium. Notwithstanding the more or less frequent occurrence of the foregoing pathological changes, we may conclude with Murchison that "there is no obvious lesion constant in or peculiar to typhus."

Treatment.—In the recognition of the facts that destitution, overcrowding, and deficient ventilation vastly increase the predisposition to typhus, lies the key to the preventive treatment or *prophylaxis* of the disease. Personal cleanliness, an abundant supply of good, wholesome food, strict temperance, a sufficient cubical air-space per head of the population (at least 500 cubic feet), and free ventilation, which means the supply of 3000 cubic feet of fresh air per head every hour, are the best preventives. Those sick of typhus should be treated in large airy wards or rooms, 1500 to 2000 cubic feet being allowed to each patient, and the beds should be at least six feet apart. Free ventilation is essential; indeed, whenever the weather permits, a strong current of fresh air should be allowed to blow over and around the typhus patient (1). Even in winter but little risk of catching cold exists while the fever lasts; and there is good reason to believe that an abundant access of fresh air may positively control the bronchial catarrh and other pulmonary affections of typhus, which result not from cold, but from passive hyperæmia of the bronchial mucous membrane and of the parenchyma of the lungs; lesions which really belong to the more essential pathology of the disease.

Bearing in mind the early and grave prostration of typhus, the patient should take to bed as soon as possible in a cheerful, large, airy apartment with two bedsteads in it, one for day and one for night. The best form of bed is a hair mattress laid upon a woven wire spring mattress. The bed-clothes should be light and frequently changed. The patient's head should be kept as cool as possible, but his feet should be warm. There is no disease in which the services of a trained, experienced, strong and judicious nurse are more needed than in typhus. Both in hospital and in private practice the nurse or nurses, for there should be a day-nurse and a night-nurse, should keep a written record, at stated intervals previously arranged, for the information of the physician, of the times at which food and stimulants have been given, the bowels have moved or water has been passed, of the changes in the nature and character of the symptoms from visit to visit of the physician, and of the behaviour of the temperature and the rate of the pulse and respirations. In all bad cases, with profuse eruption, the entire surface of the body should be gently sponged twice or three times a day with equal parts of vinegar and warm or tepid water.

So far as the physician himself is concerned, every case of fever should be visited at least twice a day—morning and evening—during the acute and critical stages; for a few hours may mean life or death to the sufferer. The condition of the heart and lungs, of the kidneys, and of the bladder, should never fail to engage the physician's closest attention.

The medical treatment of typhus is purely symptomatic, for as yet we possess no specific for this disease, if we except fresh air. Murchison employs a striking metaphor when he says, "A patient with typhus is like a ship in a storm; neither the physician nor the pilot can quell the storm; but by tact, knowledge and able assistance, they may save the ship."

While we endeavour to sustain the vital powers of the fever patient by appropriate food and stimulants, we should avoid anything which would cause congestion, or put an additional strain on organs already overtasked and with impaired functions.

The food should be both nutritious and digestible, consisting of such articles as milk, eggs, beef tea, veal broth, chicken broth, mutton broth (strained), meat essences, meat jellies, arrowroot, sago, bread and milk, custard, tea or coffee well diluted with milk. If there be a tendency to diarrhœa the milk should be boiled, or lime water should be given with it in the proportion of one part in four, or vermicelli, gelatine (isinglass), or arrowroot should be added to the milk or broth. If the digestive powers are very weak the food may be peptonised, the object of this process being to convert insoluble proteids, or albuminoids, into soluble peptones.

Food should be given to the fever patient at regular intervals—every three hours, every two hours, or even every hour; but the stomach should be allowed to rest for at least the last-named interval, else nausea, vomiting, flatulence and diarrhœa may be caused through non-assimilation and decomposition of the food. When a patient remains in a state of stupor he should be roused from time to time to take food; a teacupful of black coffee is often most beneficial. If the patient fall into a tranquil sleep after a period of wakefulness, nervous excitement, or delirium, he should not be aroused merely because the hour for food has come round. In delirium, or when the patient is unconscious or unable to swallow, liquid nourishment should be introduced into the stomach by a long tube passed through the nares, or nutrient enemas should be administered. In the latter case the rectum should first be washed out by a clyster of warm water, and then an enema should be given of milk and brandy, or beef tea, or egg flip, at a suitable temperature (100° F.), and of moderate volume (not exceeding four to six ounces).

Very few fever patients can digest more than one pint of animal broth, and from one and a half to two pints of milk, in the twenty-four hours; and these quantities seem to be a fair allowance for an adult.

The thirst of fever is the expression of a real want in the system—it is a craving for more water. The question then arises, How may water be supplied to the typhus patient? Taken internally water is the most effectual assuager of consuming thirst, the best and safest diuretic, diaphoretic, aperient and eliminative we can prescribe. Its administration in moderate quantities, at frequent intervals, often allays delirium and induces sleep. Another way in which water may be given is in the form of ice, sucking fragments of which is most grateful to the conscious and non-delirious patient. Ice, however, sometimes leaves a parched feeling in the mouth, and children are apt to dislike it. In such cases, it should be used to cool the beverage which the patient takes to allay thirst.

To wash out from the system the retained products of increased tissue change in typhus is one of the most pressing indications for treatment. It is safely and efficiently fulfilled by the internal administration of water. There can be no doubt, also, that in fever water is absorbed by the skin when tepid sponging is practised, or the patient placed in a warm, tepid, or even cold bath.

Following the practice of Dr. Stokes, at the Meath Hospital, Dublin, cold affusion may be used; the modified plan being adopted of pouring cold water from a large jug over the head and face of a typhus fever patient while lying crossways in bed, his head and shoulders being supported over a bath placed alongside the bed. The stream of water should be directed upon different parts of the head from time to time; otherwise pain may be caused. Ice also may be applied to the head—a piece, rubbed smooth with the hand, being placed in a cup-shaped sponge of convenient size. By inverting the sponge the ice is brought into contact with the shaven scalp, and is passed round and round the head by a continuous gentle motion. In this way no pain is caused, the process is grateful to the patient, and the whole head is uniformly and gradually cooled.

The question of the exhibition of alcoholic stimulants in typhus is an anxious one. The chief indications for their use are derived from the state of the pulse, the heart, the tongue and the brain; from the presence of complications, and especially of the "typhoid" or "ataxic state" (that is, stupor, low muttering delirium, tremor, subsultus, involuntary evacuations, coma-vigil, etc.) Alcoholic stimulants are doing a typhus patient good if under their use—

1. The heart's action becomes stronger and less rapid, and the first sound more distinct, and the impulse increases in strength.

2. A soft, compressible, undulating, irregular, or intermitting pulse becomes fuller, stronger, and more regular in rhythm and volume.

3. A dry, brown, or black shrivelled tongue (*parrot tongue*) becomes clean and moist at the edges.

4. Delirium lessens, the patient becoming more tranquil, or even falling asleep.

Medicinal stimulants are most urgently required during the night and in the early morning, when the vital powers are wont to flag. In the forenoon they are less necessary. In cases of extreme prostration medicinal stimulants or tonics should be combined with wine or spirits; for example, carbonate of ammonium and bark, the different ethers, camphor, musk, turpentine, quinine, and strychnine. Murchison considered, and rightly, that patients under twenty years of age do best as a rule without any alcohol, whereas most patients over forty are benefited by it after the first week of the fever. The effect of each dose should be carefully watched and noted; and stimulants must never be ordered as a matter of routine or apart from a sense of grave responsibility on the part of the physician.

In former days musk enjoyed a high reputation as a diffusible stimulant and antispasmodic in the low muttering delirium and nervous prostration of the ataxic state. In Ireland, however, of late years this remedy has fallen into disuse, perhaps, unmerited, partly because of the great cost of the drug, and partly, it is to be feared, because its exhibition was often postponed until too late to prove of much use. Certain it is that in an epidemic of typhus in Leeds in 1866, Dr. Clifford Allbutt found musk a most valuable remedy when exhibited in 5-grain doses in low delirium. It may be prescribed in bolus or emulsion.

Camphor may be substituted for musk in hospital practice. Among the various ways in which it may be administered, the method by hypodermic injection should be mentioned. A solution of camphor in almond oil, of the strength of 1 in 10 (10 per cent), may be injected subcutaneously, and will be found most useful as a stimulant, and at the same time a hypnotic and calmative. So far back as 1878, Dr. Eugene Wittich described camphor as an excellent remedy for the sleeplessness of melancholia in female lunatics. After the subcutaneous injection of 0·1 to 0·2 gramme of camphor, he found that the patient quickly became drowsy, and soon went off into a sleep of several hours' duration. He dissolved the camphor in sweet almond oil (1·0 to 10·0 grammes). The injection is less painful than one of morphin, and abscesses never occur afterwards. The canula must be rather wide, otherwise the oil does not flow readily.

Although many patients pass through typhus in safety without alcohol, there can be no doubt that its judicious exhibition may save life. It may even be necessary to prescribe it at an early stage of the fever, in cases where the occurrence of great prostration of nervous energy is foreseen. Under such circumstances the physician gives stimulants *by anticipation*. In adopting this anticipative treatment by stimulants (Stokes) we follow the old maxim, "*venienti occurrere morbo*," and we take into account the character of the prevailing epidemic and the previous medical history of the patient.

The management of some of the complications and sequels of typhus calls for a few remarks:—

Pulmonary congestion and *bronchitis* are best treated by external means—poulticing, dry-cupping, and the application of rubefacients and stimulating liniments, like compound camphor liniment, acetic turpentine liniment, and so on. Iodine may be applied as an oleate, or in combination with water and glycerine. Internally, quinine deservedly takes first place among remedial agents. It may be given in doses of five grains every three, four, or six hours, until symptoms of quinism show themselves. Digitalis may be combined with quinine; and so may tincture of nux vomica, or liquor strychninæ, or liquor arsenici hydrochloricus. In convalescence iodide of potassium and bark form a suitable and often valuable combination. Free stimulation is needed in many cases—the spirits, whisky and brandy, are more reliable than wine.

Paresis after the fever requires a generous diet, the mineral acids as tonics, strychnine, and massage with galvanism or faradisation. To these remedies shower-baths and (in summer and autumn) sea-bathing may be added. Tincture of perchloride of iron is an excellent remedy in incontinence of urine.

When *convulsions* threaten or occur, the bowels should be freely moved by a dose of calomel or croton oil, the state of the bladder should be attended to, and congestion of the kidneys should be relieved by dry-cupping and poulticing, the hot air bath, or the hot wet pack; while their action is promoted by copious draughts of water, saline diuretics, and digitalis. Wet-cupping has been practised with success for the relief of convulsions. Alfred Hudson, in 1837, recorded a case of recovery after two severe fits of convulsions in typhus after the abstraction of ten ounces of blood from the neck by wet-cupping and purging with calomel.

Bed-sores may be avoided by careful nursing, and by using a water-bed or a woven wire mattress. The threatened parts should be kept scrupulously clean and dry. They may be painted twice a day with a solution of one part of sheet gutta-percha in eight parts of pure chloroform, or equal parts of white of egg and rectified spirit, or equal parts of collodion and castor oil. When bed-sores have formed and are sloughing, they should be washed and dressed antiseptically. Carbolised oil (2½ per cent), or a mixture of two parts of castor oil and one of balsam of Peru, may be applied on lint as a stimulating dressing. Boric acid freely dusted over the cleansed bed-sore is an excellent antiseptic. These dressings should be covered with a layer of oiled silk or protective; or by a poultice less septic than linseed meal, such as the yeast, carrot, chlorine or charcoal poultice.

Phlegmasia dolens and *thrombosis* of the veins of the lower extremity are best treated by raising the affected limb on a gentle incline, enveloping it in wadding, and applying a long wide flannel bandage from the foot upwards. Strips of lint, smeared with equal parts of glycerine and extract of belladonna, may be laid along the hard, painful, cord-like swelling, which indicates the presence of thrombosis, and covered with the flannel swathe as before.

Œdema of the lower extremities generally yields to a generous diet and tonics, such as iron, quinine and strychnine.

During **convalescence** from typhus the patient should be warned against assuming the upright position too soon, and against exposure to cold. The returning appetite should be controlled for the first two or three days. After that, should the tongue be clean and the pulse quiet, a piece of boiled white fish, or chicken, or the central part of a tender mutton chop may be allowed. Costive bowels should be relieved by sipping water in mouthfuls frequently, or by the administration of enemata of cold water. Tonics may be given with advantage; but of these the most effectual are exercise in the open air, and change to the country, the sea-side, or the mountains.

J. W. MOORE.

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J. W. M.

DENGUE

SYNONYMS.—*Dengue* (derived, according to Hirsch, from the Spanish equivalent of the English word "dandy," according to Corre, from some Hindustani word—possibly *danga*); *dandy fever*; *polka fever* (Brazilian); *three days' fever*; *bouquet* (corrupted *bucket*), on account of the eruption; *giraffe* or *stiff-necked fever*; *exanthesis arthrosia*; *rheumatismus febrilis rheu-*

maticus; scarlatina rheumatica; plantaria. These are but a few of the many more or less fantastic names which, from time to time, have been given to this disease.

Definition.—A specific infectious fever peculiar to warm climates; occurring usually in widespread epidemics: it extends with great rapidity, and attacks a very large proportion of the inhabitants of the affected areas. Individual attacks are characterised by suddenness of onset; rapidly developed, quickly subsiding fever; intense headache and loin-ache; severe rheumatoid pains in or about joints and muscles; an initial erythematous and a terminal rubeoloid eruption, and a very low mortality.

History and Geographical Distribution.—Being almost entirely confined to tropical countries, rarely visiting Europe, and having but an insignificant mortality, we cannot wonder that, although very probably this disease has existed for ages, there are no records from ancient times which we are justified in regarding as applicable to dengue. Nor, for similar reasons, is it at all likely that the records available for the medical historian suffice to complete the list of the epidemic and local outbreaks even of later times since the specific features of the disease were definitely formulated.

The first recognisable descriptions of what must have been epidemic dengue refer to 1779; for in that year we have trustworthy accounts of its occurrence in Cairo and also in Batavia. It would appear that these particular outbreaks were only a part of what, so far as regards tropical and subtropical countries, was a vast pandemic wave; for in that and the following years we hear of a disease, apparently the same, in places so far apart as India (1780), Philadelphia (1780), and Spain (1784-1788). With the exception of a limited outbreak at Lima in 1818 we do not again hear of dengue until 1824. In that year, and in 1825, it was again extensively epidemic in India and at Suez; and from 1826 to 1828 it prevailed in the western hemisphere in the Southern States of the Union, in Mexico, in the West India Islands, and in the north of South America. From that time, and for nearly twenty years, we only hear of scattered and local epidemics about the Arabian coast (1835), at Calcutta (1836 and 1844), Bermuda (1837), Cairo (1845), Cawnpore (1847), and Senegambia (1845-48). From 1845 to 1849 it was epidemic in Brazil. In 1850-54 it spread to the United States and the West Indies, while about the same time (1853-54) a similar epidemic passed over India. In 1870-75 a fresh epidemic wave, starting apparently from the east coast of Africa in the neighbourhood of Zanzibar, spread all over the tropical parts of the eastern hemisphere. In 1872 it reached China, where, at Amoy, during the months of August and September, I had an opportunity of becoming practically acquainted with the disease. There appears to have been a corresponding but more limited epidemic in America confined to Louisiana. Minor epidemics occurred in Tripoli in 1878, on the Caribbean coast of North America in 1880, in New

Caledonia in 1884-85, in Fiji in 1885, and in Tripoli in 1887. One of the latest and best recorded epidemics is that described by du Brun (*Rev. de Médecine*, 1889-90), which in 1888 and 1889 spread all over Syria, Asia Minor, and the Ægean shores of Greece and Turkey.

From a study of the dates of occurrence of these various epidemics it would seem that this disease tends to assume pandemic characters once in about every twenty years. Independently, however, of the great outbreaks many minor epidemics occur in the intervals: moreover, it is asserted by some authorities that after epidemic visitations dengue tends to become permanently established as an endemic disease in certain countries where, as it is supposed, it was formerly unknown. Thus it is said to have become endemic in Egypt since 1845; in Tripoli since 1855; in Cyprus and on the Syrian coast since 1861. As an endemic disease it is believed that dengue is more common in the West Indies than elsewhere.

Besides the countries already referred to, dengue is met with from time to time in the islands of the Pacific—Tahiti and the Hawaiian group, for example; and also on its eastern shores, as at Callao and Lima.

Speaking generally, therefore, its ordinary limit of diffusion may be set down as lying between 32° 47′ N. (Charleston in South Carolina and Lodiana in India) and 23° 23′ S. (San Paulo in Brazil); but occasionally during warm weather it may spread farther north to 36° 10′ (south of Spain), 39° 96′ (Philadelphia), and even to 42° N. (the southern shores of the Black Sea).

Characteristics and Spread of Dengue Epidemics.—The most remarkable feature about epidemic dengue is the rapid way in which it spreads through a community, and the large proportion of individuals it attacks. So rapid is its diffusion that it may be described as bursting upon a place. Both in suddenness of epidemic rise and in the large numbers attacked it is comparable to influenza. In regard to the latter feature—the numbers attacked—we find that in most epidemics hardly any one is spared; all ages, both sexes, all races, and every condition of life are affected indiscriminately. Seventy-five per cent, therefore, is not too liberal an estimate of the proportion of the population attacked during an epidemic outbreak.

The epidemic which I witnessed in Amoy in 1872 was no exception in these respects to the general rule. About the first week in August cases of an unfamiliar disease were reported in the town; by the end of the second week such cases were numerous, whole families being prostrated by it at a time; a week later such cases were still more common; and by the end of the month so numerous were the invalids that the business of the town was seriously interfered with. All the patients and attendants in the native hospital were attacked one after the other. By the end of the following month, that is about eight weeks from the incidence of the epidemic, all the susceptible in the town of Amoy had passed through the disease. The epidemic hung about the place for a month or two longer, being kept alive, apparently, by strangers from such neighbouring towns and villages as had hitherto escaped the visitation. This seems to be the course of all dengue epidemics.

Like other infectious epidemic diseases, dengue tends to advance along the trade routes and lines of communication. Thus the epidemic of 1870-73, starting from Zanzibar, first reached Aden: from this port it was diffused north to the Red Sea coast and to Port Said, and east to Bombay, Calcutta and Madras, whence it radiated all over India. Passing to Singapore it followed the trade routes south to the islands of the Eastern Archipelago, and north to Siam, Cochin-China and China. From India it was carried by coolie immigrants to Mauritius and Réunion in 1873.

Influence of Climate, Season, Temperature, and Altitude.—When dengue spreads beyond its ordinary geographical limits—as, for example, in the case of the epidemics in Philadelphia, Spain, Syria, etc.—these extensions occur only during the hottest part of the year, in late summer and early autumn. Hitherto such epidemics have been arrested by the approach of winter. Even when occurring within what may be designated as its normal geographical limits, dengue prevails principally, although not invariably, during the hottest part of the year. High temperature, therefore, seems to be one of the conditions it demands.

Epidemics occur indifferently during either the dry or the rainy seasons. The hygrometric condition of the atmosphere is therefore without a manifest influence on the disease.

It would appear that dengue, like yellow fever, prefers the coast line, and the deltas and valleys of great rivers, to the interior of continents; although to this rule, just as in the case of yellow fever, there have been exceptions; such as the epidemic of 1870-73, which spread all over India. Distribution and concentration of population on the sea-board and along rivers, and the freedom of communication between communities so placed, may have some influence in determining this clinging of the disease to such localities.

As a rule, elevated places enjoy at all events a relative immunity; if the disease be introduced into such localities, usually it does not spread. To this, again, there are exceptions, for the Syrian epidemic prevailed in places from 4000 to 5000 feet above the sea-level as well as on the coast.

There are no facts, therefore, to associate the diffusion of epidemic dengue with meteorological conditions other than that of high temperature. Nor does it appear to be influenced in any way by the mineral or hygrometric character of the soil.

High temperature, a certain density of a susceptible population unprotected by the immunity conferred by a recent epidemic, and the diffusion of a specific germ by human intercourse seem to be the conditions necessary for the establishment of epidemic dengue.

Symptoms and Course.—An attack of dengue may be preceded for a few hours by feelings of malaise; or perhaps painful rheumatic-like twinges in a limb, finger, toe, or joint may herald its approach. Usually, however, the disease sets in quite suddenly. A patient, describing his experience in this respect, said that in the morning he got up as usual, feeling quite well and began to dress, but before he could complete his toilet he was so prostrated by pain and fever that further exertion was impossible, and he had to crawl back to bed. Similar stories, illustrative of the suddenness of incidence of the symptoms, circulate during every epidemic of dengue. Sometimes the fever is ushered in by a feeling of chilliness, or even by a smart rigor; sometimes a deep flushing of the face is the first thing remarked.

However it may begin, fever rapidly increases; the head and eyeballs quickly begin to ache excessively, and some limb or joint, or even the whole body, is racked with peculiar, stiff, rheumatic-like pains which, as the patient soon discovers, are much aggravated by movement. The loins are the seat of great discomfort, amounting in some cases to actual pain. The face—particularly the lower part of the forehead, around the eyes, and over the malar bones—becomes suffused of a deep purple colour; and often the skin over part or the whole of the body, and all visible mucous membranes, are more or less flushed, the mouth and throat becoming sore from congestion and small superficial ulcers. The eyes are usually much injected; very often the whole face is bloated and swollen. This congested, erythematous state of skin constitutes the so-called "initial rash."

These symptoms becoming in severe cases rapidly intensified, the patient in a few hours is completely prostrated; his pulse has risen to 120 or more, his temperature to 103°, in some cases to 105°, or even 106°: he is unable to move owing to the intense headache, the severity of the pains in limbs and loins, and the sense of febrile prostration. The skin, for the most part hot and dry, may be moistened from time to time with an abortive perspiration. Gastric oppression is apt to be urgent, and vomiting may occur. Gradually the tongue acquires a moist, creamy fur, which, as the fever progresses, tends to become dry and yellow.

In this condition the patient may continue from one to three or four days, the fever declining somewhat after the first day. In the vast majority of cases this, the first and most acute stage, is abruptly terminated about the end of the second day by crisis with diaphoresis, diarrhœa, diuresis, or epistaxis. When epistaxis occurs the relief to the headache is great and immediate. On the occurrence of crisis the erythematous condition of the skin rapidly subsides, if it have not already disappeared. In some cases crisis does not occur, but the fever slowly declines during three or four days. Thus the urgent symptoms for a time abate, and the patient rapidly or slowly passes from what in many cases may be described as the agony of the first stage to the comparative comfort of the second.

When the second stage is thoroughly established, and the temperature has sunk to normal, the patient is usually sufficiently well to leave his bed or even to attend to business. An occasional twinge in the leg, arm or finger, or a tenderness in the soles of the feet, and perhaps giddiness in walking, may remind him of what he has gone through, and warn him that he is not yet quite well. But the tongue cleans, appetite returns to some extent, and he feels moderately comfortable.

This state of matters continues to the fourth, fifth, sixth, or even to the seventh day, counting from the commencement of the illness. Then there is generally a return of fever, slight in most cases, more severe in others, and usually of very short duration—a few hours perhaps. Sometimes this secondary fever does not occur; very often it is overlooked. With the return of fever an eruption of a roseolar character appears. Along with the fever and with this "terminal eruption" the pains return, perhaps with more than their original severity. The fever subsides in a few hours, but the eruption, though at times very evanescent, may keep out for two or three days, being very generally followed by an imperfect desquamation. It seldom happens that the fever or pains of this stage keep the patient in bed, although that is the best place for him if a comfortable and speedy convalescence be desired. Rarely does the thermometer rise to 103°; it falls rapidly below the normal line on the setting in of diaphoresis, diarrhœa, or other form of crisis.

The terminal eruption possesses very definite characters. It is absent in a very few only; it is quite possible that in many of those cases in which it was supposed to be absent it was slight and had been overlooked. As stated, it is roseolar in character, and usually commences on the palms and backs of the hands, extending for a short distance up the forearms. Its development is often associated with sensations of pricking and tingling. On the palms of the hands the spots are at first about the size of a small pea, circular, dusky red, and sometimes slightly elevated: they are best seen, however, on the back, the chest, upper arms and thighs. In these situations they appear at first as isolated, slightly elevated, circular, reddish brown, rubeoloid spots from one-eighth to one-half of an inch in diameter, thickly scattered over the surface; each spot being isolated and surrounded by normal skin. After a time the spots enlarging may coalesce in places; thus irregular, red patches, from one to three inches in diameter, are formed. Or perhaps there is a general coalescence of spots, isolating here and there patches of sound skin; in this case the islands of normal skin give rise at first sight to the false impression that they constitute the eruption—a pale eruption on a scarlet ground. In a few instances, indeed, the whole integument may be covered by one unbroken, continuous sheet of red. The rash is usually most profuse on the hands, wrists, elbows and knees, and generally coalesces in these situations; there it may often be detected when absent or scanty elsewhere. The spots disappear on pressure; they never become petechial, or only in very rare cases. They fade in the order in which they appear; first on the hands and wrists, then on the neck, face, thighs and body, and last of all on the legs and feet. Desquamation may go on for two or three weeks. In many it is trifling in amount; for the most part it is furfuraceous; rarely the epidermis peels off in flakes of any magnitude, and never in the broad sheets seen after scarlatina; often, for a day or two, it is accompanied with intense irritation.

In some instances the disease may be said to finish its course with the fading of the terminal eruption. Appetite and strength gradually return, and the patient, after a few days of debility, feels quite well again and able for work. But with many, indeed with most patients, their troubles do not end so soon. For days or weeks some muscle, tendon, or joint is the seat of the peculiar pains, which may become so severe as to send their victim back to bed again. Sometimes, three or four weeks after all apparent trace of the disease had vanished, a joint or a muscle will be suddenly disabled by an attack of this description. This may occur in patients who during the acute stage suffered perhaps but little or no pain. A finger, or toe, or a joint of a finger or toe, may alone suffer. Of the joints perhaps the knee is most frequently affected, but wrists or shoulders also are often attacked; and the associated muscles may even undergo considerable atrophy from enforced disuse. The soles of the feet, too, and the tarsal articulations are favourite sites. The pains of dengue, both those occurring during the initial fever, and those which may be regarded as sequels, are difficult to locate with precision; the joints or muscle affected may be percussed, pressed, or moved with impunity. Du Brun locates those associated with the knee in the thigh muscles, which, he says, are painful on deep pressure. The pains usually are worst on getting out of bed in the morning, and on moving the affected part after it has rested for some time. They are relieved somewhat by rest and warmth. Passive movements are not painful, but any resistance to the movement of a limb may cause acute suffering. When a muscle is affected the pain is accompanied by a sense of powerlessness.

Convalescence may be very much delayed by the persistence of the pains; by anorexia, general debility, sleeplessness, evanescent feverish attacks, boils, urticarial, lichenoid and papular eruptions, and by troublesome pruritus. Among sequels and complications may be mentioned enlargement of the lymphatic glands, particularly the superficial cervical; orchitis, possibly endo- and pericarditis, hyperpyrexia, and hæmorrhages from the mouth, nose, bowel or uterus. Miscarriage is rare. The urine sometimes contains a trace of albumin, but nephritis does not occur.

Such, briefly, is a description of the dengue observed by myself in Amoy in 1872. It would appear, however, to judge from the published descriptions, that there is considerable variety in the symptoms of this disease in different places and in different epidemics. Thus certain authors mention swelling of one or more joints as a common and prominent symptom; also metastasis of the pains, enlargement of the submaxillary glands, orchitis, and so forth, as being frequently present. These in my experience were very rare. However it may be, the essential features in well-marked cases are practically very much alike everywhere and in all epidemics; nearly all writers accentuate, as leading and characteristic symptoms, the suddenness of the rise of temperature, the initial stage of skin congestion, the pains, and the terminal eruption.

Relapses of dengue are not uncommon, and second and even third attacks during the same epidemic have been recorded. As a rule, the susceptibility to this disease is exhausted by one attack.

The incubation period seems to be somewhat variable. It is certainly not a long one. I have seen a case in which it could not have exceeded twenty-four hours. Some observers place it at five or even seven days, but this is an over-estimate. One to three days seems to be near the truth.

Epizootics concurrent with dengue epidemics have been noted in Spain in 1784, and at Baroda and Rangoon in 1872. The animals affected are said to have shown symptoms of paresis of one or more limbs.

Diagnosis.—The diseases most likely to be confounded with dengue are rötheln, scarlatina, measles, syphilitic roseola, influenza, rheumatic and malarial fevers. A knowledge of the distinctive features of these various diseases, and of the fact that dengue is attended both with a rash and with articular pains, and that it occurs in great and rapidly developed epidemics, should prevent any serious error in diagnosis.

Mortality and Prognosis.—In uncomplicated dengue the direct mortality may be said to be almost nil. In the case of very young children convulsions or delirium may occur and cause some anxiety; and in the aged and infirm, and in those suffering from chronic exhausting disease, an attack of dengue may prove a serious complication. Charles describes a pernicious form which, though rare, was very much dreaded in Calcutta; in these cases the lungs were œdematous, and the patient, becoming drowsy and cyanotic, quickly passed into a condition approaching hyperpyrexia and died. Some writers state that the gravity of any given case is in direct proportion to the abundance of eruption; others deny this. In the European in hot and unhealthy climates an attack of dengue very often leads to a condition of debility necessitating temporary change of climate, or even a return to Europe. In both Europeans and natives the attendant lowering of the resistive powers disposes to other and more dangerous diseases, such as malaria, yellow fever, dysentery, phthisis, and so forth. Consequently dengue, otherwise a benign disease, may become a source of public danger. It is probable that it is in this indirect way that the general mortality rises during the epidemic visitation of this disease.

Nature of Dengue.—There can be little doubt that dengue belongs to the same class of diseases as measles, scarlatina, and the other exanthematous fevers. Analogy distinctly points to this. Certain writers, however, oppose this view; principally on the ground that the epidemic extension of dengue is so rapid and so wide that there can be no time for the operation of infection from person to person. Such writers invoke some vague telluric or atmospheric influence to explain the rapid extension of the disease in epidemics, and the tendency it exhibits from time to time to become rapidly pandemic. But if we bear in mind the shortness of the incubation period, the almost universal susceptibility of a population unprotected by a recent visitation of the disease, the frequency of mild attacks, which, even during their height, do not incapacitate the subject of them from walking about the streets and thus diffusing the infection far and wide, and the marked tendency it shows to prevail especially in towns and densely-populated quarters, one can readily understand that the entire population of a city may be exposed to and acquire the disease within a fortnight of the importation of the first case. Dengue in this respect closely resembles influenza. A highly infectious, but not in all cases nor generally a very disabling disease, to which nearly every one is susceptible, and which has a short incubation period, is bound to spread rapidly when introduced into thickly-populated districts.

As to the nature of the poison or germ of dengue there are no well-established data on which to base a very definite opinion. Bacteria, of course, have been described in connection with this as with every other fever, but the value of the observations is at best doubtful. Probably the germ of dengue resembles those of the other infectious fevers, which, with the exception of that of relapsing fever, are still hypothetical. It is a singular and suggestive circumstance that, although some of these exanthematous fevers prevail and spread during the cold season in the tropics as readily as during the hot, there are others—yellow fever and dengue—which cease at once to extend when the temperature of the atmosphere sinks below a certain point. Conversely there is one fever, common enough in cold and temperate climates, which seems to be killed down by the high temperature of the tropics, namely, scarlet fever. As the temperature of the human body is fairly uniform in all climates, any restraining influence which high or low temperature may exert on these disease germs can only operate when the said germs are outside the body, and as they pass from one person to another. The fact that these germs are so easily killed, or rendered inert, by insignificant differences of atmospheric temperature during what must be but a momentary exposure, seems to tell very strongly against the supposition that these organisms are bacteria; for such bacteria as we know are organisms which, for the most part, possess great powers of resistance both to high and low temperatures, and are certainly in all cases well able to withstand such inconsiderable elevations and depressions of temperature as occur naturally either in the temperate or in the tropical zones. Analogous and similarly suggestive contrasts in their heat-resisting capacities are supplied by the malaria germ, and by the hypothetical germs of beriberi and rheumatism.

Treatment.—Were it possible to secure perfect isolation for an individual during an epidemic of dengue there can be little doubt that he would escape the disease. Even comparative isolation is attended with diminished liability. In Amoy, in the epidemic of 1872, those foreigners who lived in a more or less rural and isolated situation were very much less affected than were those who lived in the Chinese town, or than those whose occupations threw them much in contact with the natives. This and similar facts point to the theoretical possibility of thus avoiding dengue during an epidemic; but in the ordinary circumstances of life in the tropics such precautions would be impracticable.

Like the allied fevers dengue runs a definite course; it is useless to attempt to abort or cut it short. The patient should go to bed as soon as he feels ill, and he should keep his room until the terminal eruption has quite disappeared and he feels well again. Ten days is not too long to allow in severe attacks. As in influenza, rest, light diet, and the avoidance of chills conduce powerfully to a speedy and sound convalescence. At the outset of the fever some saline diaphoretic mixture with aconite may be prescribed perhaps with advantage. If the pains be severe and the fever high, antipyrin, or antifebrin, or belladonna will give great relief. Cold applications to the head are comforting. If the temperature rise to 105° or over, cold sponging or the cold bath ought to be used. If the pains continue very distressing, a hypodermic injection of morphia will afford welcome relief and do no harm. Purgatives and emetics should be avoided, unless pronounced constipation or a history of a recent full meal urgently demand their exhibition; the pain caused by the disturbance of the patient more than counterbalances any advantage they might otherwise bring. The diet during the fever must be liquid; afterwards light and nutritious. Wine in the early stages is not advisable. Freshly-made lemonade and iced water will be found to be the most acceptable drinks during the fever.

For the pains experienced during convalescence, rubbing with an opium or belladonna liniment, gentle massage, electricity, salicylates, small doses of iodide of potassium, and quinine, have each been advocated. Debility and anorexia indicate tonics such as quinine, strychnine, mineral acids, vegetable bitters, and change of air.

PATRICK MANSON.

Hirsch's *Handbook of Geograph. and Hist. Path.*, vol. i., New Sydenham Soc., 1883, contains a very complete bibliography of dengue. The most recent important work on the subject is that by Du Brun, referred to in the text.

P. M.

YELLOW FEVER

SYNONYMS.—English, *Hæmagastric pestilence*, *Black vomit;* Latin, *Febris flava*, *Typhus icterodes;* French, *Fièvre jaune*, *Fièvre ictérode* or *amarile;* Spanish, *Fiebre amarilla*, *Vomito negro* or *prieto;* Italian, *Febbre gialla;* German, *Gelbes Fieber.*

Definition.—Yellow fever is a specific infectious disease, characterised by a continued fever of two or three days' duration; but sometimes more protracted, followed by a remission ending in convalescence; or in a state of prostration accompanied by yellowness of the skin, urgent vomiting—often of black matter, albuminuria, and passive hæmorrhages. In some cases a second febrile movement, of a remittent type, follows the remission.

Etiology. — *Endemic Habitats.* — Yellow fever is endemic in three areas—the West Indies and the adjacent coast of Mexico, the Senegambia coast of Africa, and Brazil.

Three points in particular stand out in the history of yellow fever: (i.) Its comparatively recent appearance in each of these regions; (ii.) The long intervals during which it has been absent from the places where it is most surely believed to be endemic; (iii.) The frequency with which its reappearance in the localities from which it has been absent for years can be traced to importation by ship from infected centres.

West Indies.—Hirsch may be right in regarding the epidemic disease which ravaged Guadeloupe in the year 1635 as yellow fever, for there is unequivocal evidence of its presence in this region at a somewhat later date. Du Tertre, however, who describes it under the name of *coupe de barre*, makes no reference to yellowness of the skin, to black vomit, or even to gastric irritability as symptoms in this outbreak. Violent headache, pulsation of the temporal arteries, great difficulty of breathing, lassitude, and pains in the limbs are the symptoms enumerated; and he adds that "it usually attacks those who break up the land in these islands on account of the poisonous vapours exhaled therefrom."

The first outbreak that can with certainty be ascribed to yellow fever is that which appeared at Barbadoes in 1647; and that we have here to do with the true typhus icterodes is not so much to be inferred from its having been "as killing as the plague"—for which, indeed, it was mistaken—as from the significant circumstance that it extended its ravages to the shipping in the harbour.

Yellow fever broke out in Cuba for the first time, so far as can be ascertained, in 1648-49; that is, about 140 years after the settlement of the island by the Spaniards. Making every allowance for defects in the epidemiological record, it is clear that yellow fever, if it existed at all, could not have played any important part in the pathology of the island during the first century and more after its occupation without having left some trace of its presence in the records of the time.

The first accounts of its appearance in Jamaica date from 1655; in San Domingo, from 1655; in Martinique, from 1688; at Vera Cruz, from 1690; and in St. Thomas, as late as 1793.

During the seventeenth and eighteenth centuries it was absent from all of these islands for long periods of years. Barbadoes, for example, enjoyed an immunity extending from 1647 to 1690, when the disease again broke out, and was known as "the new pestilence," or Kendal's disease. It is hardly conceivable that the inhabitants of Barbadoes would have bestowed upon it such designations if it had been then of frequent occurrence, and well known in the West Indies. Another break of 54 years occurred in this island between 1739 and 1793. In San Domingo, nothing is heard of it for the 35 years, 1746-81; and about the same period it was absent for 38 years from Jamaica. It appears to have been unknown in Cuba from 1656 to 1678; from the latter date on to 1702, and again from 1706 to 1746. Similar gaps occur in the epidemiological records of yellow fever in the other islands.

No less remarkable is the ever-recurring mention of yellow fever being carried backwards and forwards from island to island by ships. So far back as 1698, this character of the disease had become so well recognised that we find in that year a quarantine ordinance was passed in San Domingo, applying to ships coming from the Windward Islands, "in order to prevent the introduction of the *mal de Siam*," as yellow fever was then called. The frequency, too, of outbreaks seems to have borne a direct relation to the activity of trade between places within the yellow fever zone.

West Coast of Africa.—Whether yellow fever be indigenous to this coast, and was carried thence in connection with the slave trade to the West Indies; or whether, on the other hand, as upon the whole appears more probable, it was introduced into Africa from the West Indies, cannot now be determined with any certainty. There are accounts of a contagious disease at the Cape Verde Islands in 1639, which is said to have carried off 3000 men belonging to the squadron of Mascarenhas which had touched there. When this squadron reached Pernambuco in the following year a fatal distemper broke out on shore. This episode is taken by some to point to the early presence of yellow fever on the African coast. The first unimpeachable evidence of its existence in this region dates no farther back than the year 1778, when it was epidemic at St. Louis in Senegal. Schotte, who gives an account of this outbreak, states that it was not unknown in these parts, but was not an annual visitor; and he traces its introduction on that occasion from the Gold Coast by way of Sierra Leone and the Gambia—a route that we know it to have followed on more than one of the occasions on which it has been introduced from the West Indies. From Schotte's account, as well as from subsequent observations, we find yellow fever on the West Coast of Africa, as in the West Indies, being carried from place to place by maritime commerce, and having periods of outbreak followed by considerable intervals of absence.

Brazil.—As a constant element in the nosology of Brazil yellow fever dates from the last quarter of 1849, when it was introduced from Havana or New Orleans, or from both. From that time onwards deaths from the disease have been registered every year, with the exception of 1865. The annual mortality fluctuates greatly, remaining high for three or four years in succession, then sinking to a minimum.

It is from these three centres that yellow fever has been propagated to other parts of America, to Europe, to the Gulf of Guinea, to the Congo Coast, and to the West African Islands. The continents of Asia, Australia, and Polynesia have hitherto escaped this pestilence.

Area of Diffusion.—From the first of these foci yellow fever has been carried, times without number, to the Gulf and Atlantic coasts of the United States, the towns most frequently infected being seaports in constant communication with the West Indies. The seaports of the south—New Orleans, Charleston, Philadelphia, and New York—have been repeatedly ravaged by the disease; while those of New England have been invaded at comparatively rare intervals; British America indeed twice only (Quebec 1805, Halifax 1861). Natchez and Vicksburg on the Mississippi—the former 280, the latter 350 miles by water above New Orleans—have been repeatedly attacked, and a few other towns on the river and its tributaries have suffered from occasional invasions.

The Pacific coasts of Central America, cut off from direct sea communication with the West Indies, have suffered little; the only outbreaks in this region are those at San Salvador and Manzanillo in 1868, at Panama in 1884 and 1888, and at several points in the Gulf of California in 1883-84.

The northern coasts of South America—from the Gulf of Darien to Cayenne—have been subject to frequent outbreaks of yellow fever. Demerara on account of its more intimate trade relations with the West Indies has suffered most. After yellow fever became domesticated in Brazil it has thence been introduced, more than once, into Monte Video and Buenos Ayres; it has penetrated up the Parana to Corrientes and Asuncion; it was carried to Peru for the first time in 1854, where it threatened to become endemic, having maintained its footing in that country for fifteen years. Guayaquil has been invaded twice; both times, however, by way of Panama.

With the exception of an outbreak at Leghorn in 1804, all the fatal epidemics of yellow fever in Europe have been restricted to the Iberian peninsula and the Balearic Islands; and up to the time when it obtained a footing in Brazil, the disease has always been imported from the West Indies. Yellow fever made its first appearance on European soil at Cadiz, the headquarters of the West Indian trade in 1700; and subsequently invaded this port in 1730-34, 1741, 1764, and 1780. Lisbon was attacked in 1723-24, and Malaga in 1741. Respecting these epidemics it has only to be observed that, while some of them were fatal, none of them showed any tendency to spread either inland or along the coast. Very different was the case in the great Spanish outbreaks of 1800-1804, 1810-1813, and 1819-1821. These were of a more intense type, attacked almost the entire population of the invaded localities, caused a great mortality, and, exhibiting a tenacity and power of diffusion not observed in the earlier epidemics, they spread not only along the coast, but far into the interior, making great havoc in Seville, Murcia, Jumilla, and other inland cities. The later epidemics of 1823, 1828, 1870, and 1878 have been of a milder type and more distinctly localised. The last-mentioned outbreak—that of 1878—is interesting as having occurred at Madrid, and not on the seacoast as on all former occasions. It declared itself after the return of troops from Cuba, and in a street where the discharged soldiers had taken up their residence: it appeared on the 15th of September, and after attacking about fifty persons and causing thirty-five deaths it died out about the middle of October.

Lisbon, which remained free from yellow fever during the first half of the century, in the second half experienced two outbreaks—one in 1850, the other in 1856-57—after the disease had established itself at Rio de Janeiro, a port with which Lisbon is in constant communication.

Two quite insignificant outbreaks have occurred in France; namely, at Brest in 1856, and at St. Nazaire in 1861.

The only instance in which yellow fever can be said to have effected a lodgment on our shores was in 1865, when the infection was introduced into Swansea by a vessel from Cuba. Its attacks were restricted to those who had been in direct or indirect communication with the vessel, and caused fifteen deaths.

The extensions of yellow fever from the Senegambia coast have been few, and limited mainly to the African Islands. A very remarkable epidemy of what appears to have been true yellow fever occurred in 1891-92 at various military posts in Upper Senegal, 1200 kilometres from the coast. Yellow fever was not at the time epidemic in any part of Senegambia, and had been absent from Upper Senegal for ten years. Its exotic origin is thus highly improbable (1).

Endemic and Epidemic characters.—Little is known of the manner in which yellow fever is endemic in its native habitats. Is it constantly present in an attenuated form, even during the periods when it appears to be absent; is it merely kept agoing by constant importations and exportations from place to place; does it maintain its existence by the contagium being capable of remaining latent for long periods, and then, under favourable conditions, resuming its activity; or, finally, does the germ of the disease multiply and maintain itself in the soil or other substratum in the manner of a miasmatic disease? Space forbids me to enter into a detailed discussion of these questions. Suffice it here to say, that Clarac and Talairach at Martinique, and Brassac at Guadeloupe, have satisfied themselves that yellow fever occasionally reappears spontaneously, so to speak, in these islands without being imported anew. Mosny informs us that in the opinion of some of the best observers, such as Rufz de Lavison, Lota, Bérenger-Féraud, and Nielly, the bilious inflammatory fever of the West Indies, which is often epidemic along with yellow fever, is an attenuated form of the latter, and confers that immunity from the severer malady which natives and acclimatised persons enjoy (16). Direct evidence and analogy seem to favour this view.

Of the epidemic characters of yellow fever more is known. When the infection has been introduced into a locality it usually appears in single or isolated groups of cases for the first two or three weeks or longer; and these are restricted to a particular district or districts. In this, as in other respects, it reminds us of the plague. After the disease has once escaped these limits it spreads with a rapidity proportionate to the density of the susceptible population, to the freedom of intercourse between the healthy and the sick, and to the degree of temperature: and its intensity is specially favoured by overcrowding, want of ventilation, and, according to some, by an impure, undrained soil (14), and other insanitary conditions.

The duration of an epidemy is partly determined by these local conditions, partly by the season and weather, partly, again, by the number of susceptible subjects in the town or quarters of a town to which it is limited, and also, to a considerable extent, by the type of the particular outbreak.

The varying intensity of epidemies has not been sufficiently recognised. Inferences respecting the infective characters of yellow fever, drawn from observations made in ordinary years, do not apply to the seasons when the disease is so widely diffused that it may be said to be pandemic.

The maximum mortality occurs in the early autumn months (September and October in the northern hemisphere). The case-mortality is usually greatest at the beginning, and varies widely in different districts, streets, and even groups of houses. The disease is often observed to be particularly malignant in the immediate neighbourhood of the locality in which it makes its first appearance.

Agencies and Modes of Transmission.—Observation has abundantly proved that yellow fever never appears outside its native habitats or on board ship, except under circumstances that point to its introduction from without. Maritime commerce has hitherto played the principal part in its diffusion. Ships become contaminated by receiving infected persons on board, or healthy persons who have either been in an infected locality, or have had communication with an infected person: also, by means of infected clothes, baggage, cargo or ballast; and finally, by the agency of the wind, when lying in close proximity to an infected vessel.

A healthy port is infected by analogous means. It is thus that we find yellow fever breaking out on shore in the houses of sailors belonging to an infected ship, or of those who have merely visited such a vessel; attacking custom-house officers who inspect infected baggage; the labourers employed in discharging the cargo, and washerwomen who wash infected linen. Reporting to the French Government on the Cadiz epidemy of 1800, Berthe says, "On sait que ces individus (those first attacked) furent précisément ceux qui avaient eu quelque relation avec l'équipage d'une corvette Américaine arrivée depuis peu de la Havane: on sait que ces premiers malades furent ou des marins ou des hommes de peine du port, et plus particulièrement des employés de la douane et du bureau de santé" (5). Our own experience at Swansea, on a small scale it is true, was but a repetition of these observations.

When the contagion of yellow fever has been introduced into a non-endemic area the disease is spread by intercourse with the sick, or with contaminated persons, themselves healthy; by means of articles charged with the infection; by residence in or visits to infected houses: and it may be further propagated by aerial diffusion from house to house, if in close contiguity. The evidence of its communicability by means of water (24) or food, or by the agency of mosquitoes (8), is inconclusive.

It is right to say that these views are by no means universally accepted. As Hirsch points out, "the most intimate kinds of contact —such as the healthy and sick sleeping in one bed, the attendance of physicians and nurses upon the sick, the use of uncleansed linen, clothes, or beds of yellow fever patients, post-mortem examination of their bodies, and the like—have in no wise contributed to the spread of the disease." Numerous instances have been recorded which prove beyond doubt that these several kinds of contact are not necessarily followed by infection: but this is only one side of the shield. The experience of healthy soldiers occupying the same bed with their sick comrades in Gibraltar, according to Pym, was this—"the soldier was to a certainty taken ill in the course of three or four days" (17). On the occasion of the outbreak at St. Nazaire in France (1861), a shoemaker who shared his bed with a man employed in discharging the *Anne Marie* was attacked and died (2). The instances are innumerable in which those occupying the bed next to a yellow fever patient have contracted the disease. Bally, François and Pariset, for example, record the case of a young girl from Barcellonette, suffering from yellow fever, who was admitted into the hospital of Barcelona in 1811, which town up to that time had been free from fever. "Three women," we are told, "who occupied the neighbouring beds were immediately infected" (3). Jackson himself, who was strongly opposed to the doctrine of contagion, admits that many persons came under his own observation who had contracted the disease in hospitals.

Physicians, nurses, and confessing priests have in some epidemics fallen victims to the disease in great numbers. Those in the service of hospitals suffer less than those employed in ministering to the sick in their own dwellings. Fraser, referring to the epidemy at Gibraltar in 1813, notices "the early and almost universal seizure of medical officers, of the clergy and rabbis, and of those immediately employed about the sick, whether friends or attendants, and the sickening of washerwomen" (9). At Alicante in 1804, according to Pariset, out of 13 physicians, 10 were attacked and 4 died. All the surgeons of the town, 14 in number, were attacked, and 7 died. Coming down to quite recent times, we have it on official authority that 22 out of 27 physicians and pharmaciens perished in the outbreak of 1878 in Senegal. Still more conclusive evidence of the danger of intercourse with the sick is furnished by the relative incidence of the disease on the confessing and the non-confessing priests, often residing in the same monastery. From data supplied by Bally, François and Pariset, it appears that 101 out of 111 confessing priests, whose duty it was to attend the sick and dying, were seized; while 2 only out of 12 non-confessing priests were attacked.

The evidence of the communicability of yellow fever by contaminated clothes and other effects rests on two orders of facts:—First, the direct evidence derived from instances in which contaminated articles have given rise to the disease when transmitted to a distant place where yellow fever was absent; secondly, the no less cogent evidence afforded by instances in which yellow fever has been carried by healthy persons to localities perfectly free from the disease. A single instance of each of these modes of transmission must suffice. Bérenger-Féraud, after adducing several striking instances of the transmission of yellow fever by contaminated effects, says: "I know another fact at least as strange; it is that of the development of yellow fever in a remote village of the Basses-Alpes, after the parents had received clothing belonging to their son who had died of yellow fever in Senegal, and which had not been disinfected" (4).[1] Dr. Paterson, in the *Medical Times and Gazette* for 1870, records an example of the second order of facts. Bahia was free from yellow fever from September 1850 to March 1852. In the beginning of May 1851 the barque *Gipsy* arrived from Rio, where yellow fever was then raging with great intensity, having on board men suffering from the disease, and having lost men from it on the passage. The disease continued to make havoc on board after reaching the harbour until all who were susceptible had been attacked. The master of the vessel had already suffered from yellow fever in the West Indies. His wife was on board, and being immediately landed, went to reside a mile or so in the country. On the 16th June, six weeks after landing, she was seized with the complaint and very narrowly escaped with her life. She had not been on board, nor did she have any communication with the vessel, except through her husband, who slept on shore, but passed the day on board his vessel. He himself during the whole time remained in perfect health. The infection in this case had undoubtedly been conveyed by the captain in his clothes or effects from the contaminated vessel.

For evidence of the efficacy of strict isolation in securing immunity in the midst of the infection, we must refer the reader to the works of Pym, Fraser, Arejulá, and others mentioned in the bibliography (18).

Rainfall and Humidity.—Rainfall has no influence upon yellow fever except in so far as it affects the temperature. A high degree of atmospheric humidity has been thought to increase the influence of a high temperature in favouring its spread.

Topographical and Altitudinal conditions.—Yellow fever is notably a disease of seaports and of towns situated on navigable rivers. It seldom prevails in an epidemic form in the country, in sparsely inhabited places, or at high elevations. In its severer outbreaks its diffusive powers are greater, and it does not then limit itself very strictly to coast or river. Leaving out of view the altogether exceptional explosion in Upper Senegal to which I have referred, the farthest point inland to which it has attained is Madrid, above 200 miles from the sea. It has more than once appeared at Cardoba in Mexico, 66 miles inland by rail, which again is one of the highest points it has reached, being 3045 feet above the sea-level. A few cases occurred in 1860 and again in 1867 at Newcastle in Jamaica, at an altitude of 4000 feet. This marks its extreme altitudinal limit. It has several times broken out with considerable severity at Camp Jacob in Guadeloupe, at an elevation of 1800 feet. How far the freedom of high elevations from yellow fever is to be ascribed to their lower temperature is somewhat doubtful; but that this is one of the causes of their immunity can hardly be disputed.

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[1] I see no valid objection to Lind's statement that yellow fever was introduced into Philadelphia in 1741 by means of the clothes of a person who had died of the disease in Barbadoes. It is asserted that the family of the deceased fell ill after opening the box containing the infected clothes, and from this arose an epidemy that carried off 200 persons. (Lind, *Two Papers on Fevers*, London, 1763.) I have been unable to verify this reference. For other instances of the transmission of yellow fever by clothing see Ferguson's account of its introduction into Ascension, quoted by Pym, *op. cit.* pp. 76, 77.

Soil.—Yellow fever shows no predilection for any geological formation, for any particular kind of soil, or for marshy and malarious localities. The etiological importance of an impure, ill-drained soil, apart from the usually attendant conditions of over-crowding and defective ventilation, has been generally admitted; but not on very convincing evidence. Yellow fever has been observed on some occasions to attack by preference blocks of houses built on made-up ground; and La Roche, who has collected instances of this kind, has also emphasised the upturning of the soil as a factor in yellow fever explosions (22). One is the more disposed to look upon the facts narrated as simple coincidences, inasmuch as upturning of the soil ceased to occasion yellow fever outbreaks in the Southern States from the time that effective measures for the inspection and disinfection of vessels from the West Indies came into force. When we reflect on the numerous instances in which strictly isolated communities living in the worst localities have escaped—as, for example, the 500 persons confined in the dockyard of Gibraltar in 1813 (9)—while the disease was raging around them, we cannot avoid the conclusion that, in temperate climates at least, the soil has very little to do with the spread of yellow fever. It is in the house itself and its contents, rather than in the soil on which it is built or by which it is surrounded, that we have to look for the lurking-places and breeding-places of the infection.

Personal conditions.—*Age and Sex.*—In the Lisbon epidemy of 1857 it was ascertained that out of 3466 deaths 2061 were of males and 1405 of females. The age distribution per 1000 was as follows:—

Years	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90
	26	116	212	194	166	152	94	31	9

These figures show that yellow fever is more fatal to men than to women, and to adults than to children. As it generally assumes a milder form in women than in men, the difference in the ratio of attacks between the sexes is considerably less than that in the mortality.

Race and Acclimatisation.—The susceptibility of the white race to yellow fever is much greater than that of the negro; and the disease in the former assumes a more fatal character than in the latter. In epidemic years, however, the immunity of the negro is less conspicuous. Rush observes that in 1793 the Africans "took the disease in common with the white people, and many died of it," but he adds that "the disease was lighter in them than in the white people" (23).

The observations of Blair in British Guiana and of Barton at New Orleans place it beyond doubt that the natives of colder latitudes pay a heavier tribute to this malady than those born in warmer climates. Blair found the mortality per 1000 of those attacked, according to nationality, to be as follows: West Indians, 69; Italians and French, 171; English, 193; Germans and Dutch, 202; Scandinavians and Russians, 277. In the same way it has been shown that natives of the south of France are less liable to be attacked than those of the north.

As persons born in a yellow fever country suffer less than strangers, so foreigners who have resided for some years in a place where it is endemic are very much less susceptible than new-comers. Rey found that no less than 80 per cent of attacks occurring in foreigners at Rio in 1876 fell on those whose residence in the city was under one year. This incidence of the disease on new-comers is analogous to the liability of the soldier fresh from England to contract typhoid fever in India and other tropical countries. We cannot refuse, then, to admit for acclimatisation an important and significant place in the etiology of yellow fever.

One developed attack of the disease ensures immunity for life: exceptions to this rule are extremely rare. When yellow fever reappeared at Gibraltar in 1813 there were about 5000 persons within the walls who had already been affected. None of these, so far as could be ascertained, suffered a second attack.

Remote Causes.—Fraser informs us that, among the troops stationed at Gibraltar, it was observed that the hard drinkers and debilitated were those most severely affected. "Almost all the first victims at Baltimore in 1794 were persons habituated to the immoderate use of ardent spirits, and very few of them recovered." Excesses of all kinds, fatigue, exposure to the sun's rays, and depressing mental emotions are enumerated as entering into the causation of yellow fever.

Relapses during convalescence, although not common, are full of danger. They are usually to be traced to indiscretions in diet or exposure to cold.

Incubation.—The period of latency in yellow fever may be put down as ranging between twenty-four hours and four or five days. The length of time elapsing between the date of exposure and the declaration of the disease, which does not necessarily correspond with the period of incubation, has been known to extend to forty-five days or longer.

Bacteriology.—None of the micro-organisms that have, from time to time, been announced as the specific germ of yellow fever have been proved to be causally related to it; and the claims of the two that have attracted most attention, namely, the *Cryptococcus xanthogenicus* of Freire, and the *Tetragenus febris flava* of Finlay, have been disposed of by Sternberg. Some good observers have hitherto failed to detect microbes in the blood, kidney, liver or nerve-centres. Dantec found several varieties of micro-organisms in the black vomit, and in the mucous membrane of the stomach and intestine. None of these has been proved to be the cause of yellow fever. Some interesting attempts have been made by Rangé to transmit the disease to dogs, rabbits and other animals, by inoculation with blood and black vomit. The results appear to be inconclusive: it has still to be proved that the blood, black vomit, or alvine discharges contain the infective agent of yellow fever. One case only which seems to incriminate the discharges of yellow fever patients is known to me: Bérenger-Féraud states that a physician contracted yellow fever in Paris in the winter of 1873 while studying yellow fever dejections. I have not seen the original paper (*Gaz. Méd. Nantes*, 1883) which contains the details of this case.

Nature of the Disease.—The fact that the introduction of a single case of yellow fever into a healthy locality is enough to diffuse the disease through a large community, proves that the contagion becomes multiplied as in other infectious diseases. Where does this process of increase take place? Is the infective agent reproduced in the body of the sick, and given off from it? Or is the yellow fever patient, as Hirsch suggests, a medium of spreading the disease only in so far as the morbid poison clings to him as it does to other objects; and that in this respect he plays no other part than his effects, or the coffers in which he keeps them, or than ships or utensils? (11). In the first case, yellow fever will take its place among the contagious or the miasmatic contagious diseases; in the second, it must evidently be classed among the purely miasmatic maladies. No doubt many of the circumstances of its propagation, as well as the almost complete immunity conferred by an attack, seem to indicate a relationship to the contagious class of diseases; and the opinion that, under certain circumstances, it may be contagious, like small-pox and measles, cannot be entirely excluded until the micro-parasite of the disease has been isolated and its life-history studied. It is almost impossible, however, to conceive of a purely contagious disease being restricted (as we know yellow fever in most instances is) to seaports, and often to certain limited districts of a town.

Still more does yellow fever differ in its mode of propagation from the miasmatic contagious diseases, such as cholera and typhoid fever. In these the virus is present in the evacuations, and is generally communicated to the healthy by the agency of water or food contaminated with fæcal discharges, and never, I apprehend, by temporary proximity to infected persons or things; far less by the intermediary of healthy persons. Whether yellow fever be communicable by water is doubtful; but that air, and not water, is the common medium by which it is communicated is certain. If we cannot positively say that the vomit and fæces of yellow fever patients are innocuous, we are quite sure that the disease is not dependent for its propagation on either. Linen from the sick need not be soiled by vomited matters or fæces in order to become infectious.

That yellow fever is essentially a miasmatic disease can hardly admit of doubt. On this hypothesis, we explain the innumerable instances in which the disease has been communicated by contact with, or proximity to, the sick, by assuming that the patient's clothes or surroundings are charged with the miasm; this becomes diffused through the air, and is either directly so conveyed into the system of a healthy person in the vicinity, or clings to the clothes of the latter, and these afterwards communicate the infection either to the wearer of the clothes himself or to others. If these infected articles of dress are packed away in a close and warm place, a centre of infection may be set up to give rise to an explosion of the disease weeks or months afterwards, which may affect those who have not been in direct communication with the sick. This miasmatic theory harmonises with the well-known tendency of the virus to cling to houses, to the holds of ships, to clothes and other media; and renders intelligible the slow initial development of an epidemy, its seasonal character, its reappearance in a town after having been latent during the winter, and the influence of acclimatisation in diminishing susceptibility.

Granted the varying intensity of the infective agent, for which I have contended, the miasmatic theory explains alike those facts that have been appealed to in support of the non-contagious nature of the malady, and the equally well-attested evidence of its transmission by contact with the sick, by the agency of fomites, and by breathing the air of infected houses.

Symptoms and Course (General sketch).—In quite exceptional instances a certain degree of malaise, characterised by anorexia, constipation, headache, or vertigo, is felt for a day or two before the attack. Much more frequently yellow fever declares itself abruptly, seizing the patient without warning while in his usual state of health.

The first symptom is usually a chill, which may amount merely to a feeling of coldness so slight and evanescent as scarcely to attract attention; or it may be more intense, declaring itself in a rigor, severe but of short duration, or by repeated shiverings alternating with heats. In some cases the chill is absent. This stage of invasion seldom lasts above twelve hours, and its intensity and duration are often observed to bear a direct relation to the severity of the impending attack. Severe frontal and ocular headache, racking pains in the loins and limbs, pallor of the skin, and a rise in the temperature, are the usual symptoms of the invasion stage.

As the chill passes off, the face becomes red and turgid, and the eye injected and brilliant; the headache and the pains in the loins, joints, and muscles of the extremities increase in intensity. The patient is agitated and anxious; the mind may remain clear, or at most wanders at night: in rare cases only is there active delirium. The temperature in the meantime rises rapidly, generally attaining its fastigium within twenty-four or thirty hours from the onset of the disease; and reaches some point between 103° and 107° F. according to the severity of the attack. The respiration is hurried and laborious, and the pulse accelerated, full and bounding. The skin in the milder cases is moist, but in the severer it is dry and pungent. The appetite is lost; the tongue is covered with a white fur, the tip and edges being red; the bowels are constipated; there is a sensation of heat, pain, or distress at the epigastrium; the stomach becomes irritable, and vomiting of a clear acid fluid ensues. The urine is scanty, and from the second day is found to contain albumin, while the urea is diminished.

On the second or third day—sometimes later—a change takes place. The temperature and pulse fall; the headache and pains subside; the characteristic redness and turgidity of the face tone down, as does also the suffusion of the eye, which in many cases now assumes the yellow tinge which may afterwards extend to the rest of the body. The gastric irritability and distress likewise abate, and the patient feels better.

This is the turning-point in the disease. If the improvement is to end in convalescence, the temperature falls gradually to the normal; the gastric distress disappears and the appetite returns; the urine increases in quantity, while the albumin steadily diminishes and a corresponding increase of the urea takes place.

If, on the other hand, after a lull extending from a few hours to one or two days, the gastric symptoms reappear in an aggravated form, with thirst, anxiety at the præcordia, and vomiting of a clear liquid mixed with chocolate-coloured flakes, or of a fluid uniformly black, the patient's life hangs doubtfully in the balance. These symptoms are accompanied either by a recrudescence of the fever or by, what is more ominous, a fall of the temperature below normal; and by a diminution of the urinary secretion, with a corresponding increase of albumin.

Yet even at this stage a change for the better may take place. In this case the irritability of the stomach again subsides, the patient's strength rallies, a gradual amelioration of the other untoward symptoms follows, and convalescence is rapidly established. More frequently, however, the balance inclines the other way. The prostration increases; copious vomiting of black matter sets in; the yellowness of the skin becomes more pronounced and generalised; in the more malignant cases the skin is likewise covered with petechiæ and vibices; and along with these, and depending upon the same conditions, hæmorrhages often take place from the mucous membranes. In some epidemics gangrenous spots on the limbs or on the scrotum have been of relatively frequent occurrence. While these ominous symptoms are being evolved the mind may remain clear and continue so till the end. More frequently the patient, though not incoherent, is apathetic; he fails to realise his condition; expresses himself hopefully as to his state; lapses from time to time into a dreamy reverie, or attempts to get out of bed. Towards the end hiccup sets in, the features become shrunken, subsultus tendinum appears, and the patient dies exhausted or comatose.

Grades and Forms.—The most useful classification is that which recognises three grades of intensity—the mild, the severe, and the grave; and arranges anomalous forms separately under the heading of pernicious.

The gravity of the third grade depends upon an exaggeration of one or more of the common symptoms of yellow fever; as when, for example, the fever rises to a point that puts life in jeopardy.

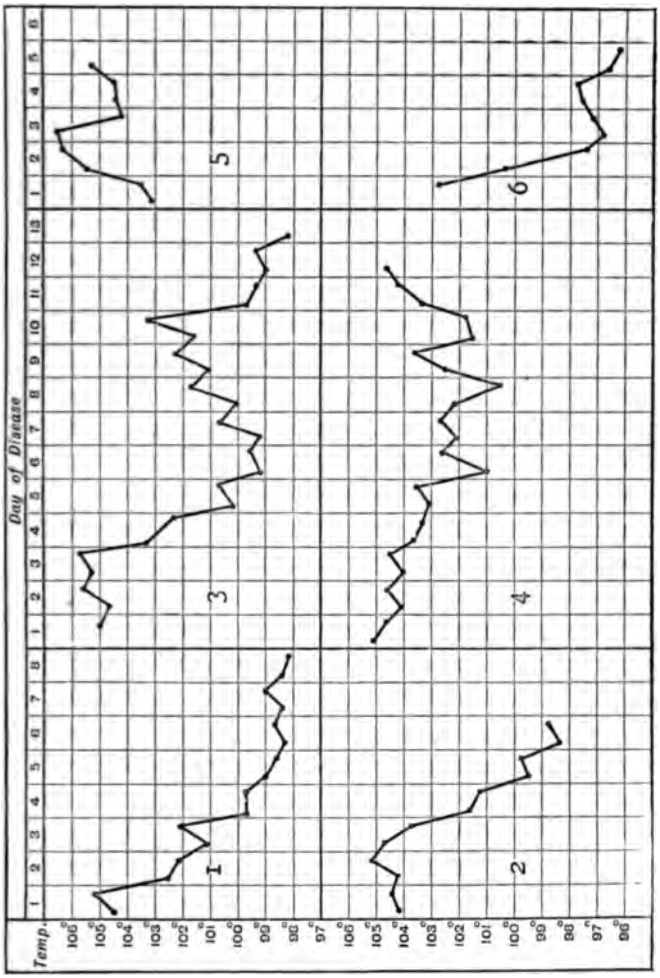
The pernicious forms, on the other hand, are distinguished by the development of some special symptom or group of symptoms foreign to the ordinary phenomena of the disease. I shall restrict myself to the briefest notice of three of these:—

1. *The Apoplectic Form.*—The patient is more or less suddenly struck down with vertigo followed by stupor, coma, and convulsions, generally terminating in death. The pulse is weak, and finally becomes faltering and irregular; the skin is cold and clammy, or dry and flabby. "In the meantime the patient lies as if stunned, with dilated pupils and an expression of gloom upon the countenance. From this unpromising state an effort at reaction occasionally takes place, but this scarcely ever leads to a successful result. More generally the patient becomes perfectly comatose; the eyes assume a glassy appearance, the pulse fades away, involuntary discharges and profuse hæmorrhages supervene, and death soon ensues" (La Roche).

2. *The Algid Form.*—This form was of rather frequent occurrence in the epidemy of Lisbon in 1857. The prostration is early and extreme, the features are sunken, the surface cold, and in severe cases this coldness extends to the lips, tongue, and breath. The temperature in the axilla often falls to 96° F. The pulse is small or imperceptible. In a large proportion of these cases the hæmorrhagic tendency is present in an extreme degree. Yellowness of the skin is very often wanting, and, when it does appear, is generally limited to a slight yellow tinge of the conjunctivæ.

3. *The Choleraic Form.*—This form is marked by excessive purging and vomiting, copious clammy perspirations, petechiæ scattered over the skin, and great prostration. An interesting account of an epidemy which occurred at Curaçoa is given by Rouppe (14), in which excessive bilious vomiting and purging, with copious cold sweats and intense prostration, replaced the ordinary symptoms of the invasion stage.

Analysis of Symptoms.—The *temperature* in yellow fever is marked by a sudden rise to 104° or 105° F. The fastigium is generally attained in twenty-four to thirty-six hours, and the temperature continues at this point, with slight variations, for a period of two or three days; sometimes longer. It now falls by degrees, steadily or with evening exacerbations, to or within a degree or two of normal. When a remission only takes place, this evening rise and morning fall are frequently observed before the temperature finally attains the normal; and at this period a second rise may set in, also characterised by distinct morning remissions and evening exacerbations, seldom ranging above a degree, a degree and a half, or at most two degrees Fahrenheit. This secondary rise is only met with in the more severe forms. Although considerable uniformity is observed in the evolution of the febrile phenomena in most cases of a mild or moderate grade, it must be confessed that the march of the temperature, especially in the grave and pernicious forms, is often very regular. The following chart illustrates some of the characters of the mperature curve to which I have alluded :—



Pulse.—During the stage of reaction the pulse is accelerated, full, unding, and compressible; diminishing in force and frequency as the mission sets in. In grave cases it is small, fast, and feeble, and towards e end irregular and intermittent. It may be observed that there is no rrespondence between the number of pulsations and the height of the ermometer.

The *skin* is pale during the period of invasion, and when algid symptoms anifest themselves this state of pallor continues and develops into lividity. When reaction is established the skin becomes hot and dry, or hot and moist. It is often hot and dry at the outset, and becomes moist or covered with perspiration as the reaction advances. The face is now red and turgid, and the eye suffused and brilliant. Yellowness of the skin is often absent in mild cases throughout the whole course of the disease; and, strange to say, it is often wanting in the algid form, even when hæmorrhages are present. It is rarely altogether absent in the more intense grades of the disease; although in these, too, it may be so little obtrusive as to be overlooked, while in other instances the skin assumes a deep orange or even bronze hue.

Icterus seldom makes its appearance before the beginning of the remission, when the redness of the face has subsided. In some cases its advent is deferred until the approach of death, or it may not appear until after death. The yellowness is first noticed on the conjunctivæ and face, spreads to the neck and chest, and then to the rest of the body. True hepatogenous jaundice, with bile pigment in the urine, and decoloration of the fæces, is to be regarded as a purely accidental phenomenon. In yellow fever the icterus is hæmatogenous, and closely associated with albuminuria.

Petechiæ and large irregular purpuric patches are met with especially in the algid and hæmorrhagic forms.

An erythematous eruption on the scrotum, or around the vulva, is frequently observed; and, when present, is looked upon as pathognomonic of yellow fever.

An altogether indescribable odour, which is occasionally exhaled from the skin in malignant cases, is a sure prognostic of death.

Hæmorrhages are occasionally, but very seldom, seen in the early part of the pyrexial stage. They are of most frequent occurrence at a later period, that is, after the remission has set in; they are most extensive in the malignant forms, especially the algid, and are undoubtedly more common in some epidemics than in others. The more numerous and abundant they are the graver is the prognosis; death in the more distinctly hæmorrhagic forms usually taking place from the fifth to the seventh day. The most common form of hæmorrhage, of course, is the black vomit,—a serious symptom, it is true, but much less so than the generalised hæmorrhages with which we are now concerned. Besides the purpuric spots and patches that are often the first signs of a hæmorrhagic tendency, we meet with bleeding from the nose, lips, and gums, from the whole gastro-intestinal tract, from the uterus and vagina, from the bladder and urethra, more rarely from the bronchial mucous membrane, and from the ear and conjunctiva. Extravasations of blood may also take place into the interior of the eye and destroy vision.

White, Red, and Black Vomit.—Vomiting is a very general symptom of yellow fever. It begins with the vomiting of an acid, colourless or bile-tinged, and more or less viscid fluid; this may be distinguished as white vomit. In the milder cases this alone is ejected, and this is also what is met with in the febrile stage of those severer cases in which, after the remission, black vomit appears.

The red vomit of Cunisset is simply gastric hæmorrhage; in this case the blood is expelled immediately after its escape from the vessels, thus retaining its red colour.

Black vomit, which gives its familiar name to the disease, and is justly invested in the popular mind with the most gloomy associations, is absent in a majority of the milder cases; and seems, even when present, to be less fatal in some epidemics than in others. It makes its appearance during the period of remission. Often after a deceptive lull, gastric distress and irritability reappear, and vomiting supervenes; first, perhaps, of a clear acid fluid containing dark-coloured flocculi, then of a uniformly black fluid, ejected often in large quantities, and with considerable force: it is composed of altered blood, which, on standing, deposits a black sediment —the supernatant fluid being of a clear or slightly brownish colour. *Microscopically*, black vomit consists of glandular epithelium, mucus cells, deformed and often decolorised red cells, yellow pigment granules, fat globules, granular débris, and various kinds of micro-organisms. The colouring matter of the blood in black vomit, according to Dantec, is present in the form of hæmatin. Its *chemical* composition varies greatly. Its acidity is mainly due to hydrochloric acid. Cunisset in numerous analyses failed to detect in it urea, the biliary acids or salts, or cholesterine. The ptomaines of black vomit isolated by Lapeyrère deserve further study.

The urine in yellow fever is generally acid; its density varies with the amount of albumin that it contains. The quantity voided, which is diminished from the onset of the disease, becomes still more scanty during the period of depression; and in cases tending to a fatal issue complete suppression often occurs.

Albumin makes its appearance during the febrile stage, the amount bearing a direct relation to the severity of the attack. The urea is notably diminished, and the uric acid to a less extent. Blood is present in the secretion when there is hæmorrhage from the kidney, bladder, or urethra.

Stools.—Constipation is the general rule during the febrile stage. In some epidemics bilious or choleraic diarrhœa has been of frequent occurrence. In favourable cases the bowels resume their normal action when the remission sets in. Obstinate constipation, or diarrhœa with melæna, are alike dangerous symptoms at this stage.

Pathology.—*The blood* in yellow fever coagulates loosely or imperfectly, and this condition becomes more marked as the disease advances. Recent analyses show that the fibrine ranges from 1·80 to 2·10 per 1000 at an early stage of the disease, and from 0·50 to 0·80 per 1000 after death. Many of the red and white corpuscles are normal in size and shape; the latter, when preserved in culture cells, have even been observed by Sternberg to retain their characteristic movements for twenty-four hours. Numerous red corpuscles, on the other hand, are seen to be crenated, and the white cells are often granular. These alterations are most marked in the advanced stages of the disease. The serum is yellow in colour from the presence of free hæmoglobin. According to the analyses made by Cunisset, 100 grammes of serum contain, in the first period, from 0·005 to 0·013 of hæmin; 0·004 to 0·012 of hæmatin; 0·10 to 0·30 of hæmoglobin, and 0·09 to 0·27 of globulin. After death the proportions are—0·04 to 0·09 of hæmin; 0·038 to 0·086 of hæmatin; 0·95 to 2·15 of hæmoglobin, and 0·87 to 1·97 of globulin. These figures indicate a rapid destruction of the red corpuscles which cannot be ascribed to the presence of biliary salts, which indeed are seldom to be detected in the blood even in small quantities.

Brain and Cord.—The more constant morbid alterations met with in the nerve-centres are congestion of the meninges and, to a less extent, of the substance of the brain and cord; and effusion into the subarachnoid space and cerebral ventricles. Minute hæmorrhagic points are not infrequently observed in the pia mater and brain. Fatty degeneration of the capillaries and, according to Lobo, of the cells of the gray substance is present both in the brain and cord. Inflammatory effusion on the arachnoid covering the pia mater has been occasionally noticed. The ganglia of the sympathetic—especially the solar plexus—show evidences of fatty degeneration.

Heart and Pericardium.—Usually no lesion is observable in the heart, if we except a dull and flabby appearance which this organ often presents in common with the muscular system generally. Minute ecchymoses, however, are sometimes met with in the muscular substance and under the endocardium. Effusions—serous, purulent, or sanguineous—are not infrequently found in the pericardium, which may also be injected, or be the seat of small petechial-looking hæmorrhages.

Stomach.—Morbid alterations, more or less pronounced, are always met with in the stomach, whatever the period at which death occurs. More or less of a black fluid, similar to black vomit, is almost always present in the cavity. The mucous membrane is irregularly congested in patches or bands, but the hyperæmia is less marked in patients who succumb at an advanced period of the disease. Small ecchymoses are also frequently met with. The mucous membrane is often softened.

Under the microscope the superficial venules and capillaries are seen to be engorged, the latter undergoing fatty degeneration. The tubular glands are variously deformed and atrophied, and their epithelium is in a state of fatty degeneration. The submucous connective tissue is comparatively intact; although here and there points of congestion may exist, and inflammatory infiltration may also be detected occasionally. Various kinds of microbes have been found in the walls of the stomach and intestine, but their nature and relation to the disease have not been established.

Intestinal Canal.—Black matter, similar to that found in the stomach, is often present in the upper part of the canal. The contents of the intestine usually give an acid reaction. Vascular arborisations, more or less extensive, are observed, especially towards the lower part of the ileum. The solitary glands, as well as Peyer's patches, are sometimes found enlarged, and fatty degeneration of Lieberkühn's crypts has been demonstrated.

The Liver, which almost uniformly presents some shade of yellow, is generally of normal consistence and volume. It is seldom found enlarged, and the instances in which it is diminished in size are quite exceptional. On section its substance usually presents an exsanguine appearance, but when death occurs early it may be found hyperæmic. The liver cells in the peripheral lobular zone are seen to have undergone fatty degeneration, not, however, uniformly throughout the gland. The portal spaces are often infiltrated with young cells.

The spleen is not enlarged nor altered in consistence, except as the result of previous malarial disease.

The kidneys are usually of normal size, and not congested to any extent, except when death has occurred within the first three or four days. Small hæmorrhages, however, are occasionally observed in the mucous membrane of the calices and pelves, and more frequently as pin-point extravasations into the cortical substance, which on examination prove to be seated in the capsules of the glomeruli. The renal epithelium undergoes cloudy swelling and fatty degeneration. The tubes in some places are divested of epithelium, and are often filled with a hyaline or granular albuminous material. The capillaries here, as in other organs, exhibit evidences of fatty degeneration.

Mortality.—The numbers attacked and the case-mortality vary extremely in different epidemics and regions. It may be laid down as a general rule—not without exceptions—that the case-mortality stands in an inverse ratio to the number attacked. The mortality is higher in the larger Antilles and on the West Coast than in Europe, South America, or on board ship.

Berthe, who reported for the French Government, gives the following figures for the outbreak in Spain in 1800:—

	Population.	Attacks.	Deaths.	Sick.
Cadiz .	57,499	48,520	7,387	357 on 31st Oct.
Seville .	80,588	76,488	14,685	85 on 30th Nov.
Xeres .	33,000	30,000	12,000 to 13,000	...

When an intense form of the disease attacks a susceptible population comparatively few escape; especially if they are closely packed within narrow limits. Thus it happened that at Gibraltar in 1804, only 28 out of 9000 persons escaped, and nearly one-half of these had acquired an immunity by a previous attack. Pregnant women attacked with yellow fever abort and few recover.

Diagnosis.—Yellowness of the skin, albuminuria, and hæmorrhages, although very characteristic of yellow fever, are not entirely pathognomonic. They have all been met with in epidemics generally regarded as malarious, although we may remark that their malarious nature has not as yet been confirmed by a bacteriological examination of the blood. The significance to be attached to these symptoms must thus manifestly depend upon the region and circumstances in which they occur, and the type of fever by which they are accompanied. Yellow fever has a limited geographical range and its own distinctive places of election. It is also a communicable disease, usually of a single febrile paroxysm; and when a second rise of temperature follows the remission, it never exhibits the true periodicity of malarial fevers. If these features of yellow fever are kept in view the diagnosis will seldom present any difficulty.

The diseases with which yellow fever is most likely to be confounded are ephemeral fever, pernicious malarial fever with jaundice, bilious hæmoglobinuric fever, and relapsing fever.

Mild attacks of yellow fever can only be distinguished from ephemeral fever by attending to the circumstances in which the attack occurs, and by the absence of albuminuria in the latter. Malarial fever in all its forms is distinguished by the enlargement of the spleen, the periodicity of the febrile phenomena, and, above all, by the presence of the malarial parasite in the blood. Bilious hæmoglobinuric fever is paroxysmal—not continued: the porter-like urine is highly characteristic, and the liver is always enlarged. Relapsing fever is often accompanied by jaundice, and by vomiting, and occasionally by hæmatemesis and albuminuria. The discovery of the spirillum Obermeieri in the blood will set at rest any doubts that the similarity of the symptoms might occasion.

The prognosis in yellow fever must always be guarded, as unfavourable symptoms may appear when least expected. If the temperature in the first stage is moderate, the skin is moist or covered with perspiration, and the temperature falls early and reaches the normal, without any symptoms of depression; if the epigastric distress and irritability are slight and disappear with the fever; if the urine is in fair quantity, contains little albumin, and a moderate amount of urea, the prognosis is favourable.

If, on the other hand, the disease is ushered in by convulsions or severe and long-continued chills; if the temperature rises to or above 106° F.; or if, on the other hand, reaction is not at all or only imperfectly established, and algidity supervenes; if the albumin in the urine increases while the urea diminishes; if generalised mucous hæmorrhages, petechiæ, or purpuric patches make their appearance, and coffee-ground vomiting is urgent; finally, if delirium, vertigo, coma, or hiccup set in, an unfavourable issue may be feared. Perhaps the most dangerous of all these symptoms are algidity with hæmorrhages.

Prophylaxis.—Our first object, evidently, must be to ensure a thorough sanitation of the seaports where the disease is endemic, and of those menaced by their frequent intercourse with infected centres. The other measures of prevention will readily be understood from what has been said of the etiology of the disease. They include avoidance of intercourse with infected localities and persons, and contact with or proximity to contaminated things; the isolation of the sick on the one hand, and the seclusion of healthy garrisons, prisons, and asylums on the other; the complete disinfection of bed and body clothes, of contaminated vessels and houses, and of the excreta and vomit of the sick. Individual prophylaxis requires that the person shall keep out of the way of infection and avoid the predisposing causes of the disease.

Treatment.—Until the cause of yellow fever is known, its treatment must be empirical, and to a large extent directed to meet the symptomatic indications. In all cases it is important to have the patient removed from the focus of infection and treated in a well-ventilated room. In the milder forms little more will be necessary than the administration of a hot mustard foot-bath and a purgative. When the temperature is moderate, the skin moist, and irritability of the stomach absent or trifling, a meddlesome line of treatment is to be avoided. In all cases—severe as well as mild—the hot mustard foot-bath is to be employed on the invasion of the disease, and repeated once or oftener according to circumstances. Its use favours diaphoresis and tends to relieve internal congestions. The administration of a laxative or purgative, as soon as reaction has set in, is also useful alike in mild and severe cases. This treatment is indicated by the constipation which is generally present, and justified by the good effect which the concurrent testimony of physicians past and present concede to it. Although it has not been proved that the parasite of yellow fever has its brooding-place in the alimentary canal, or that the ptomaines which give rise to the phenomena of yellow fever are present in the stomach and bowels, the possibility, to say the least, that such is the case, furnishes an additional reason for the judicious use of purgatives in order to clear the *primæ viæ* of their contents—specific or otherwise. As to the purgative best adapted for this purpose there is less agreement. Castor oil has obtained the greatest number of supporters: it is best given in capsules or in the form of emulsion. When castor oil cannot be retained, ten grains of calomel, given alone or combined with jalap, may be employed. No good will be obtained from excessive purgation; but it is necessary that a free action of the bowels be obtained and kept up.

When the temperature is high and the skin dry and hot it is evidently desirable, if possible, to abate the febrile excitement. Quinine has been largely employed for this purpose; but experience has, upon the whole, decided against its utility at any stage of the disease. Antipyrin deserves a fuller trial than it has hitherto received in those cases in which the fever attains a high grade; but its effects should be carefully watched, and it is contra-indicated when the heart's action is weak and the vital powers depressed. The common saline mixture, containing acetate of ammonium, nitrate of potassium, and spirit of nitrous ether, is of service in cases of moderate intensity; it reduces the temperature to some extent and promotes the action of skin and kidney. When there is great arterial excitement, five to ten drops of tinctura veratri viridis may advantageously be added to the mixture. The Brazilian physicians, according to Rey, make use of a mixture containing infusion of jaborandi, acetate of ammonium, and tincture of aconite. When the *calor mordicans* is well marked such a combination seems indicated. It is said almost always to give rise to profuse diaphoresis and a decrease of temperature.

Whatever may be the internal treatment adopted to assuage febrile action, its efficacy will be promoted by frequent sponging of the body with cold or tepid water, and the assiduous application of cloths dipped in iced water to the head. Cold affusions, if used at all, should be reserved for cases of hyperpyrexia.

Vomiting is one of the most common, one of the most distressing, and, at the same time, one of the most intractable symptoms with which we have to deal. Dr. Macdonald informs us that in the epidemy of yellow fever on board H.M.S. *Icarus*, in the West Indies, a few drops of chloroform prepared the stomach for the reception and retention of food. As a matter of fact, in most cases, at least in the early stage, food is neither desired nor necessary; but the remedy is sometimes of service in relieving the gastric irritability which is so exhausting to the patient. Creosote, again, in drop doses mixed with mucilage and sugar, deserves a trial. It was frequently found by Blair to moderate or check vomiting. I may mention a few out of many other remedies that have been recommended for this purpose by men of experience and ability. Oil of turpentine in doses of ten drops every two hours in syrup was used by Dr. Physick and Dr. Rush; the latter administered it with success even in the last stage of the disease. Opium and subcutaneous injections of morphia over the epigastrium have also been employed; but the use of opium in any form, although it undoubtedly allays the gastric irritability, is not devoid of danger, and it has been discarded by most practitioners. Nitrate of silver, in the dose of one-eighth to one-third of a grain, has seemed in some instances to relieve vomiting and to check hæmorrhage. It may be said of all these remedies that if they have sometimes proved successful they have more frequently failed. The best results have been obtained from the use of antacids, and of these lime water, in doses of three or four ounces with an equal quantity of milk (which may be given iced), has been found most generally of service. Fluid magnesia, and bismuth with bicarbonate of sodium, have both been used with advantage. If antacids fail, small morsels of ice should be swallowed from time to time. A large sinapism should always be applied over the epigastrium as an important adjuvant to internal remedies.

In the third stage, when the vomiting is urgent and the prostration is extreme, recourse must be had to iced champagne, given frequently in moderate doses. If the feeble and irregular pulse indicates that the heart is failing, fifteen to twenty-five minims of ether may be injected hypodermically over the epigastrium or elsewhere.

Gallic acid, perchloride of iron, and ergotine have been employed to check hæmorrhages. It is useless to expect much success from their use in this dangerous complication, but it is an encouragement to know that recovery in very hopeless cases has sometimes followed their employment. In the Lisbon epidemy of 1857 (20) perchloride of iron was given with apparently good results in arresting the hæmorrhages.

Sternberg's Treatment.—We are indebted to Surgeon-General Sternberg for a method of treating yellow fever which has been followed with great success. His formula is as follows:—Bicarbonate of sodium, grs. 150; bichloride of mercury, gr. $\frac{1}{3}$; pure water, oz. 40. Three tablespoonfuls of this mixture are to be taken, ice-cold, every hour. This treatment has been found to check gastric irritability and to increase the urinary secretion. Whether it owes its virtue to the antiseptic properties of the bichloride it is unnecessary here to inquire. The principal point is, that the mortality in 374 cases, treated by ten physicians in the United States, Cuba, and Brazil, was only 7·3 per cent. If further experience should confirm these results the terrors of the disease will largely disappear.

Alimentation.—If milk and lime water be given to control vomiting, this will furnish amply sufficient nourishment during the febrile and remission periods. If Sternberg's treatment be adopted, he recommends that nothing be given for the first three or four days: he then allows an ounce or two of iced milk, or of chicken broth, every two or three hours. A return to solid food is to be cautiously sanctioned only as convalescence is established. When vomiting, with or without fever, follows the remission, the difficulty of maintaining the sinking powers becomes extreme. Iced beef tea or milk, with or without lime water, must be given at short intervals and in small quantities. If the stomach reject all food, resort must be had to nutritive enemas; and these are all the more likely to be retained and absorbed, as in yellow fever the large intestine is seldom affected. This is now the time for the exhibition of stimulants. Iced champagne, in particular, sometimes proves beneficial, but this luxury is often beyond the means of the patient; brandy or whisky, diluted with iced water, will be more generally available, and is often well retained: the amount and frequency of the dose must be regulated by the condition of the patient, the way in which it is tolerated, and its observed effects.

Andrew Davidson.

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A. D.

DYSENTERY[1]

Synonyms.—Gr. Δυσεντερία, from δύς, difficulty, and ἔντερον, the bowel; Lat. *Tormina, Dysenteria;* Eng. *Dysentery, The bloody flux;* Fr. *Dysenterie, Ténesme, Flux de sang;* It. *Dissenteria, Flusso;* Span. *Disenteria, Camaras de sangue;* Ger. *Ruhr, Die rothe Ruhr;* Swed. *Rœdsot.*

Definition.—Until a firm etiological or pathological basis of classification be obtained, we must content ourselves with determining the limits of our subject rather than attempt a strict definition of the subject.

Our clinical conception of acute dysentery is that of an inflammatory disease of the large intestine, with or without fever, characterised by mucous, serous, or bloody stools containing epithelium, débris, or sloughs of the bowel, accompanied by tormina and tenesmus.

This definition must be accepted, however, with some qualifications; for it includes diseased conditions with which we, in this chapter, have no concern—such as amœbic dysentery, toxic and secondary dysenteries, and some local inflammatory processes due to obstructions and other mechanical causes; while, on the other hand, it excludes cases which, presenting themselves under the guise of diarrhœa, are nevertheless mild cases of dysentery. These mild or abortive forms are frequent in every outbreak in temperate and tropical climates. The milder and severer forms of diarrhœa are met with side by side; they merge into each other, the inflammatory type of diarrhœa being indistinguishable from the milder degrees of dysentery. In individual cases, too, dysentery often arises out of what seemed to be an attack of simple diarrhœa; so that no hard and fast line can be drawn between diarrhœa and dysentery.

The difficulties in the way of an accurate clinical definition of dysentery are not obviated if we qualify the inflammation as "specific." The doctrine of specificity is itself vague. Some assume that a single specific microbe, hitherto undetermined, underlies all forms of the malady;[2] others, with better reason, incline to the view that more than one pathogenetic agent is capable of producing the severer forms of the disease.[3]

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[1] The Editor regrets that by an oversight of his own in the first volume (p. 503) "Dysentery" was omitted from the class of Endemic Infections, and "Amœbic Dysentery," escaping from the "Diseases due to Protozoa," took its place. The two diseases are now described in their proper order.

[2] "Le développement de la dysenterie est dans tous les cas subordonné à l'intervention d'un agent unique et spécifique."—Courtois-Suffet, Charcot's *Traité de méd.* t. iii. p. 531.

[3] "Möglicher Weise kommen verschiedene Formen derselben (bacteria) in Betracht, doch ist das specifische Ruhrvirus bisher noch nicht sicher nachgewiesen."—Birch-Hirschfeld, *Lehrbuch der path. Anat.* Bd. ii. 1895.

That such specific agents do exist can hardly be doubted by those who have witnessed dysentery in its epidemic or endemo-epidemic manifestations; but, until their existence is demonstrated they cannot be used as a basis of classification. Moreover, the ordinary micro-organisms of suppuration, putrefaction, and sepsis, in various combinations, as we shall afterwards see, play an important part in all forms of dysentery. This fact renders it probable that any agent, specific or otherwise, whether parasitic, toxic, or mechanical, which materially impairs or destroys the vitality of the intestinal wall, may bring the tissues into a state in which they become the prey, if I may so express it, of the pus, gangrene, and sepsis exciting organisms which are everywhere present and ever ready to lay hold on partially devitalised tissue: thus a "dysentery," in the etiological acceptation of the term, is set up.

From the standpoint of morbid anatomy, again, dysentery includes various toxic, secondary, and mechanically produced forms of colitis and proctitis, which fall to be dealt with elsewhere. The clinical definition, then, of dysentery, with the inclusive and exclusive qualifications, given above, will serve sufficiently to indicate the forms of disease to be treated of in this chapter.

ETIOLOGY.—**Forms of Dysentery.**—It will be convenient to consider the causation of dysentery: A, in its epidemic; B, in its endemic manifestations; and, C, as it presents itself in connection with war and famine. The terms "sporadic" and "endemic," as applied to dysentery, indicate nothing more than varying degrees of prevalence—the former variety, if such it be, will therefore be included in the latter. Sporadic cases, however, occur constantly in connection with epidemic dysentery.

This arrangement does not proceed upon the assumption that these forms are distinct entities, but is adopted merely because it has the advantage of enabling us to bring into relief certain peculiarities in the origin, mode of spread, and pathological affinities of the forms that deserve notice.

A. Epidemic Dysentery.—*Features.*—True epidemic dysentery, which must be distinguished from the endemo-epidemic outbreaks with which it is frequently confounded, appears at irregular intervals, sometimes in widespread epidemics, embracing regions equal to the half of Europe; more frequently it occurs in outbreaks restricted to a kingdom or province, sometimes it is confined within limits purely local. There is no reason for supposing that these outbreaks, differing as they do in extent, are not of the same nature and due primarily to the same cause or causes. The local outbreaks are liable to be confounded with limited extensions from endemic foci, and from want of detail in the records it is often impossible to distinguish between them.

Range.—Epidemic dysentery, as I have defined it, is generally restricted to the colder temperate regions.

In the great European epidemics of 1538, 1717-19, 1779-83, 1834-36, 1846-48, 1853-55, the disease was generally restricted to Northern and Central Europe. Twice only do we hear of Italy being invaded by the disease; namely, in 1538 and in 1787. In the former instance the Italian outbreak was probably an incident of war. Spain and Portugal appear to have been usually spared when the northern kingdoms have suffered.

The same predilection for the temperate regions of the globe is to be found in its outbreaks in North America in 1749-53, 1773-77, 1793-98, and in 1847-56, when it was most diffused in the Northern States, and, so far as is known, did not extend to the tropics, or prevail to any extent in the Southern States.

Such accounts as we have of it from the southern hemisphere point also to the temperate zone as the region in which it prevails. It has been observed more than once in South Africa—the most fatal explosion there occurred in 1804. For the southern parts of the western continent we have it on the authority of Sigaud that epidemic dysentery is principally met with in the southern provinces. That the Arctic regions are not quite exempt from epidemic outbreaks is proved by the fact that dysentery has been three times epidemic in North Greenland during the eighteenth century.

We have some accounts, however, of epidemic dysentery from the Society Islands and the New Hebrides which deserve notice. These islands, it may be observed, are within the tropics, although their climate is rather that of temperate regions. Ellis records that after a visit from Vancouver's ship to the Society Islands in 1790, dysentery appeared among the natives and "proved fatal to a large portion of the population." It is not stated whether dysentery was present in the vessel. In this century this group has again been visited by the same disease, which "swept through the islands, and carried off numbers of the people."

Epidemic dysentery appeared in Futuna, one of the New Hebrides group, in 1842, and caused a great mortality (8). The circumstance of its latest occurrence there in 1893 has peculiar interest, having been witnessed by Dr. Gunn, who, along with his wife and two children, suffered from the disease; the children died of it. It was introduced, he tells us, by a labour vessel from Sydney (1400 miles distant), which landed a Futunese woman and her half-caste child suffering from dysentery. The disease soon spread and carried off one-fourth of the population. One of the most remarkable things in connection with these Oceanic epidemics is that dysentery, in its endemic form, is prevalent both in the Society and the New Hebrides groups. It would seem, then, as if some pathogenetic agent were present in the stools of the child suffering from the Australian form of the malady, which, if it exist at all in the endemic dysentery of the island, is present only in an attenuated form.

These epidemics are not observed to take their departure from foci where the disease is endemic. They frequently begin about the same time at different centres, as was the case in the United States in 1847. From these centres the disease spreads outwards in successive years, while it is diminishing in prevalence and dying out in the localities first attacked.

A Seasonal Disease.—Like all miasmatic or miasmatic-contagious maladies, epidemic dysentery is a seasonal disease. It becomes dormant during winter and spring to revive in summer, and to attain its maximum prevalence and fatality in autumn (5).

Relation to Soil, etc.—The configuration of the country, the nature of the soil, and altitude of the locality, have little influence on the spread of the disease. The facts that these outbreaks frequently last over a series of years, and extend over wide regions, prove them to be largely independent of weather. It is to be remarked, however, that some of the most severe epidemies that have visited Europe have occurred during and after exceptionally hot summers.

Mortality.—The prevalence and mortality of epidemic dysentery vary greatly in different outbreaks; and in the same outbreak in different localities. The sudden increase in the deaths from dysentery is very remarkable when the disease becomes epidemic in a given locality. In Massachusetts, for example, the deaths from this cause, for the six years ending 1846, averaged 236 annually. In 1847 the number rose to 1074, and in 1849, when the epidemy was at its height, it reached 2455. In the Department of Neckar in Würtemberg, the cases, in 1834, numbered 167, and the deaths 17 per 1000 of the population. Mortalities even higher than this have been recorded for particular localities, but the dysenteric death-rates for an entire kingdom during a severe epidemy seldom exceed the ratio of 2 per 1000 living.

Contagion.—No one contends that epidemic dysentery is contagious in the sense that small-pox and measles are so; yet that its virus may, under certain circumstances, be conveyed by the healthy seems proved by evidence, ancient and modern, that cannot lightly be set aside. Conclusive instances of this nature were observed by Homan and Hartvig in the Norwegian epidemy of 1859. But this is certainly not the usual mode by which the disease is propagated. Innumerable instances are, however, on record in which a patient suffering from the malady has introduced it into a district previously healthy. Blanche cites a case of a dysenteric patient, transferred from an infected district into a commune perfectly free from the disease, who became the source of "a murderous outbreak, which *spread from the house he occupied.*" Numerous instances of a similar nature will be found in the records of epidemic dysentery published annually in the *Mém. de l'Acad. Royal de Méd.*; and further references to ancient and recent observations are given in Hirsch's work. Facts such as these prove that the pathogenetic agent is present in the stools, and probably multiplies in the soil, infecting water, food, and air; through these media it becomes diffused as a miasmatic-contagious disease.

B. Endemic Dysentery.—*A diminishing factor in the pathology of temperate climates.*—Changes in nomenclature and other causes forbid us to place much confidence in the figures of dysentery mortality given in the London bills of mortality; but they may be accepted at least as evidence that the disease was endemic in England in the sixteenth and seventeenth centuries, and had gradually declined so as to be met with only as isolated cases in the beginning of the nineteenth century. In the seventeenth century, for five-and-twenty years (1667-1692) the deaths in London ascribed to bloody flux and griping in the guts averaged above 2000 annually; by the end of last century they had gradually declined to about 20. Slight recrudescences have been observed in England and Scotland during this century—especially in 1826-1828, and in 1846-1848 under exceptional meteorological or social conditions.

This marked decline in the prevalence of dysentery must be ascribed to improved water-supply and sewerage, to the drainage of marshes, and to a general amelioration of the condition of the population in respect to food and lodging. In Ireland, where dysentery has always been more common than in England, it has, in the present century, been repeatedly epidemic during seasons of want; but the Registrar-General's reports show that there too, as an endemic disease, it is losing importance in each successive decade. The same decrease in the prevalence of dysentery is more or less noticeable in all civilised countries, and is especially marked in Canada and the United States. In the decade ending May 1879 the cases of dysentery admitted into the Montreal General Hospital numbered 150; whereas in the last ten years only 31 cases have been admitted.

Distribution.—Endemic dysentery becomes more prevalent, although not uniformly so, as we advance from the temperate to sub-tropical and tropical regions; and as the mean temperature of the summer and autumn months increases. In this respect it offers a contrast to the epidemic form, which, as we have seen, is seldom observed within the tropics.

Even within the limits of a country such as Italy, stretching through eight degrees of latitude, the difference in the prevalence of dysentery between the north and south is well marked. The dysenteric death-rate in the four northern departments (1881-1886) was 0·7, in the four southern departments it was as high as 5·1 per 10,000 living. The same increase towards the south holds good in France. In Nancy the ratio of deaths from dysentery to 1000 deaths from all causes is 2·4; in Paris, 6·0; in Bordeaux, 10·1; and in Narbonne, 15·2. Many exceptions to this rule exist, some of which do not at present admit of explanation. Singapore, for example, is situated within one degree of the equator; it has an annual mean temperature of 81° F., a rainfall of 90 inches, and a soil in many places swampy; but dysentery of a grave type is somewhat rare. Dysentery, again, is more fatal in Senegal (15° N.) than on the Gaboon, which is under the equator. But it is a mistake to suppose that any tropical country is free from dysentery; the worst kinds are brought into evidence in countries such as Perak and the Gold Coast when they become the theatre of war; though in them dysentery among the settled population is otherwise comparatively rare.

Relation to Soil.—In temperate climates dysentery is mostly endemic in marshy and water-logged districts. "It is thus," to use the words of Kelsch and Kiener, "that the reports of the Academy continually notice it as occurring in the various departments of Brittany, in the fluvial districts of the lower Loire and its affluents, in the basin of the Somme, on the plateaux of the Doubs and the Vosges, and in the low parts of Alsace. The southern part of Finistère, l'Ille-et-Vilaine, some districts of the Côtes-du-Nord, and above all Morbihan, have acquired in this respect a sad notoriety." In Sweden, too, in former times, dysentery found its home in the provinces occupying the central depression bordering on the lakes, and finds it there to some extent at the present day.

In keeping with this predilection of endemic dysentery for marshy localities, accounts of its endemo-epidemic extensions in temperate climates generally point to the temporary establishment of paludal conditions. Thus, in 1873, an outbreak arose from the cleaning out of the lateral canal of the Loire and the desiccation of the mud. A similar result followed at Leymen (Haut-Rhin) from the clearing out, in August 1850, of a vast slimy reservoir situated in the middle of the village. The first cases declared themselves a few days after the exposure of the mud, and occurred in the houses nearest to the reservoir; the disease propagated itself afterwards to almost all the houses in the village, dying out only towards the end of October. In the same way we explain the outbreaks of dysentery, sometimes observed along with malaria, in marshy localities in exceptionally warm seasons.

In tropical countries dysentery appears to be more independent of soil than in temperate climates, but an imperfectly drained or marshy soil is everywhere favourable to its prevalence. Dr. Maclean states, as the result of his experience, that "in India dysentery prevails most, and is most fatal on moist alluvial soils"; and this I believe is true of the tropics generally, although other elements enter so largely into the causation of the disease that apparent exceptions are numerous in all climates.

The geological nature and the mineralogical constituents of the soil are secondary in importance to its physical conditions—its dryness, humidity, and aeration. These, again, are of less moment than its state of organic purity. That a soil charged with dysenteric, or perhaps even with simple fæcal evacuations, is capable of giving rise to the disease, was amply proved by the Cumberland and Westmoreland Asylum incident of 1864. Among the causes of the frightful dysentery mortality which made Secunderabad a bye-word, none was more effective than the saturation of the soil of the site itself with organic impurities, the extreme pollution of the vicinity with fæcal matters, and the bad privy accommodation.

Relation to Altitude.—The ascent from the plains of a tropical region to the hills represents, as Bérenger-Féraud puts it, "*un véritable voyage jusqu'aux environs mêmes du pôle.*" Our voyage, however, generally falls short of securing for us the conditions met with in temperate, not to speak of polar climates. At moderate elevations, say of 3000 feet, in South India, the winter temperature still exceeds that of an English summer. The advantage gained by a decrease in the mean temperature is thus often more than counterbalanced by the increase in the range of the thermometer. The day temperature is excessively high, the nights chilly; and when the local conditions are at the same time unfavourable, there is no difficulty in understanding why dysentery should frequently be more common at such stations than along the coast.

When altitudes are attained in the tropics which reduce the mean temperature of summer to that of temperate climates dysentery diminishes in prevalence.

Relation to Malaria.—It is unnecessary at the present day to insist upon the fact that the geographical distributions of malaria and of dysentery are by no means identical. In order to demonstrate that dysentery is not always caused by malaria, it is enough to instance the island of Rodrigues, which is non-malarious, although dysentery (1887) causes 29·6 per cent of the total mortality. It is perhaps of more importance to emphasise a fact which is now rather lost sight of; namely, that, while there are many non-malarious countries where dysentery is rife, it is difficult to point to any malarious region within the tropics where the malady is unknown. In malarious regions, where, in settled civil life, dysentery is rare, it immediately steps to the front rank of fatal maladies when such a country becomes the seat of war; and the dysentery arising under such conditions is often of a very malignant kind. In proof of these important statements we have only to refer to the history of the Ashanti war of 1874, and of the American Civil War. Haspel shows how apt dysentery is to supervene in those who have been weakened by malaria. Of fifteen men arriving in Algeria from Rochefort, scarcely convalescent from fever, five died of dysentery within six months' residence. As that accomplished and revered physician Warburton Begbie pointed out in the first edition of his work, "the relation of dysentery to intermittent and remittent fevers, formerly insisted on, was not, strictly speaking, etiological, but to be accounted for by the disordered state of the portal circulation, which, occurring in ague, led indirectly to the inflammatory affection of the colon."

Relation to Season and Weather.—In temperate and sub-tropical climates, in the northern and southern hemispheres, endemic dysentery is essentially a disease of late summer and autumn; and this is the case irrespective of the period of maximum or minimum rainfall in a particular country. In tropical regions this rule does not always hold good, at least as regards the natives. Autumn is the season in India when dysentery is most fatal to Europeans; winter that in which it carries off most of the natives. The quarterly distribution of 100 deaths from dysentery in the Native Army of Bengal is as follows:—

1st Quarter.	2nd Quarter.	3rd Quarter.	4th Quarter.
28·1	13·7	19·7	37·5

The reason of this seasonal difference in the two races is, perhaps, the result of peculiarities of constitution in relation to temperature. "The constitution of the European is set for cold, that of the native for warmth."

Internal congestions, with the tendency to dysentery so engendered, are determined in the former by heat, in the latter by cold.

Most physicians who have seen much of the disease have ascribed the foremost place among the remoter causes to vicissitudes of temperature, to exposure to cold after being heated; in short, to a *chill*. Some eminent physicians, such as Rochard, still maintain that a chill alone, without the intervention of any specific cause, can give rise to dysentery. "Nothing more," he says, "is required in a warm climate to give rise to an attack of dysentery than to pass one night in the open without sufficient coverings." That continued depressing exposure to cold and wet is sufficient to bring the bowel into that depraved state in which the pathogenetic agents find their morbid opportunity cannot be doubted. Although the instance I am about to relate belongs properly to the dysentery of war, it is introduced here in order to conclude what I have to say on this part of the subject. Pringle relates how the English soldiers after a night march (June 26th 1743) fought the battle of Dettingen, and had to pass the following night on the field of battle without tents; they had afterwards to encamp on wet ground without straw to protect them from the damp. "In eight days after the battle about 500 men were seized with the distemper, and in a few weeks nearly half the men were ill or recovered." Within half a mile of this army lay a body of men who had taken no part in the fatigues of the march and the battle, and "had never been exposed to rain nor had lain wet." This body of men, although they had used the same food and had the same water-supply, almost entirely escaped the disorder. The great point to notice is, that the dysenteric germ is never wanting in any country or season when men are exposed to conditions similar to those that Pringle describes.

Relation to Water and Food.—Water is an important vehicle for communicating dysentery, and when it has in solution or suspension substances calculated to produce irritation of the bowels, it is an effective predisposing cause of the malady. Nothing in connection with the etiology of the disease is more conclusively established than this; although one recent and able authority on the subject (Woodward) appears to think that the influence of impure water has not yet been fully proved, or has at anyrate been much overrated. The two following examples should be sufficient to remove all doubts upon this point:—The troops at Cork, says Dr. Barry, suffered much from dysentery while they occupied the old barracks. "They were supplied from the river Lee, which, in passing through the city, is rendered unfit for drinking by the influx of the contents of the sewers from the houses, and is likewise rendered brackish by the tide. Mr. Bell engaged water-carts to bring water for the troops from a spring called the Lady's Well. At the same time they were forbidden to drink the water of the river. The dysentery shortly after disappeared. The poor inhabitants then had no other water, but lately a few public fountains have been established for their use; and it is certain that dysentery is not nearly so common as formerly." The endemic prevalence of dysentery at Millbank, diversified by murderous epidemic explosions as in 1823-1824, ceased from August 1854 when the prison was supplied from the artesian well in Trafalgar Square. The supply was previously obtained from the Thames as it ebbed and flowed beneath its walls. We may add that the dysentery death-rate in the Navy has fallen from 12·7 in 1860 to 1·2 in 1880, coincidently with the use of condensed water. Outbreaks due to the same causes have been repeatedly observed in public institutions.

Tainted meat or fish, food of coarse quality, unripe or over-ripe fruits, may either act as the vehicles of dysentery or, by producing intestinal catarrh, as the indirect causes of the disease. Aretæus reckons among the causes of dysentery κρεῶν παλαιῶν δριμέων ἐδωδή. Abuse of alcoholic drinks renders the body more susceptible to contract dysentery. Constipation and impaction of fæces in the colon, whether mechanically or by determining putrefactive changes in the fæces, may prove to be important causes of the disease. Annesley may have exaggerated the influence of fæcal accumulations in the causation of dysentery; but their importance has of late been much under-estimated.

Personal Conditions.—All *ages* are consistent with dysentery; but, if we exclude the dysenteric diarrhœa of children, adults are most liable to be attacked. *Sex* and *race* influence the liability to dysentery little, if at all—due allowance being made for habits and conditions of life.

Contagion.—In the tropics we never hear of nurses or others being infected from the admission of a dysenteric patient into the wards of a general hospital. Endemic dysentery is, in fact, looked upon and treated as a non-communicable distemper. It should not be forgotten, however, that in regions where the disease is always more or less prevalent, the creation of new foci would readily be overlooked; and this may account for the fact that in tropical countries one never hears of such an event. On the other hand, there are numerous conclusive and striking instances of dysentery breaking out in ships of war, which were previously free from the disease, soon after the embarkation of dysenteric patients who had contracted the malady in the tropics. We are thus warranted in believing that an infective virus is present in dysenteric stools of tropical dysentery, and may justly suspect that much of the disease in warm climates is really due to the infection of soil, air, and water by dysenteric discharges. The instances are innumerable in which the endemic dysentery of temperate climates has become epidemic; and not infrequently it has spread in a previously healthy locality after a case has been introduced from without.[1]

C. Dysentery of War and Famine.—Space only allows me to indicate in the most cursory way some of the respects in which the dysentery met with in camps, in besieged cities, and in communities suffering from famine, differs from the ordinary endemic and epidemic forms of the disease.

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[1] For instances of this kind the reader is referred to Degnerus, *Hist. med. de Dysenteria, etc., Traj. ad Rh.* 1738; *Archiv. gen. de méd.* t. v.; Schmidt's *Jahrb.* vol. ii. 1860; *Mém. de l'Acad. Ryl. de Méd.* t. xviii.; Kelsch and Kiener, *Traité des mal. des pays chauds*, Paris, 1889. For instances of outbreaks on board ship after embarking patients suffering from tropical dysentery, see Charcot's *Traité de méd.* t. iii. ch. viii. Paris, 1892.

(*a*) The dysentery of war and famine shows little respect for climate or season; under the given conditions, it appears in countries most free from the endemic disease, and at all seasons of the year. We have only to remember how it raged among our troops in the depth of the severe winter of 1854 in the Crimea, to realise how independent of season is war dysentery. There are few healthier climates than New Zealand, which enjoys an absolute immunity from malaria, but dysentery did not spare our troops there in 1862-65. The dysentery of war is not perhaps wholly indifferent to the nature of the soil. Marshy conditions appear to aggravate the malady. "At Limerick, which, as Trim says, 'lies in the middle of a devilish wet, swampy country,' many of King William's army fell a sacrifice to dysentery" (Cheyne).

(*b*) The dysentery of war and famine is extremely fatal; and it has a greater tendency than any other form to become complicated with typhus, typhoid, and malarious fevers. Typhus has been the predominating complication in Ireland and in some other countries of Europe. Malarious diseases cut off the famine-stricken dysenteric population in India; while in camps, whether in malarious or in non-malarious countries, typhoid has always manifested itself along with dysentery. The medical history of Europe and America attests the fatality of war dysentery. Famine dysentery is certainly no less destructive. In the Irish workhouses, during the ten years ending June 1851, no fewer than 50,019 perished from dysentery, and 20,507 from diarrhœa. These two diseases alone caused considerably more than a moiety of the total mortality.

(*c*) The dysentery of war and famine frequently assumes a contagious character. Pringle, continuing the medical history of the army after the battle of Dettingen, already referred to, tells us that the sick were removed to Feckenham; and that there they communicated the distemper to the rest of the patients, to the apothecaries, to the nurses, to those employed in the hospital, and to the rest of the inhabitants. Coming to recent times, Lombard informs us that dysentery appeared in every place, whatever its latitude or physical features, where the Russian troops, returning from the Crimea in 1856 and 1857, made a sojourn. Trousseau makes a similar observation for Algeria. That the same is true of the dysentery of famine is shown by the history of the epidemic at Penzance in 1848. Creighton, in his work on the *Epidemics of Great Britain*, relates how the brig *Sandwich*, carrying Irish emigrants for Boston among whom dysentery prevailed, had, through stress of weather, to put in at Penzance; there three of the women suffering from the disease were landed and died. Dysentery soon after broke out in the town and caused 105 deaths; and new foci of the disease were set up in country districts by domestics and others who, while suffering from dysentery, were sent from Penzance to their respective homes. Is it not probable that the seeds of the great epidemy, which raged in the United States from 1847-56, may have been carried from Ireland across the Atlantic in the same way? If so, the etiological unity of the dysentery of famine and epidemic dysentery would be proved.

Bacteriology.—Numerous researches have been made during recent years into the bacteriology of dysentery, some of which are not without value in their bearing upon the etiology of the disease; although they still leave the most important problems unsolved.

Ziegler, in a local outbreak occurring in Germany, observed a small bacillus, partly scattered partly occurring in masses, in the adenoid tissue of the mucosa within the lumen and under the epithelium of the crypts of Lieberkühn, and in the connective tissue; and the increase of this microbe in the tissues was accompanied by inflammation, tissue necrosis and degeneration. Here we have an undoubted dysentery bacillus, but it has yet to be proved that it is the constant or common cause of epidemic dysentery. Ogata found in the stools and ulcers of epidemic dysentery in Japan a small bacillus, with rounded ends and active movements, which formed greenish yellow colonies in plate cultures, and which produced dysentery when injected into the rectum of cats. Whether this be the organism of Ziegler, or a variety of it, is uncertain. Maggiora found in the fæces in epidemic dysentery large numbers of bacterium coli, with proteus vulgaris and other forms of bacteria. In epidemic dysentery in France—possibly of the endemo-epidemic form—Bertrand and Baucher found in the stools (α) septic anaerobic vibrios; (β) the bacillus pyocyaneus, to which they ascribe the preponderating part in the causation of the disease; (γ) the bacterium coli commune, and another organism, which they regard as a variety of the same microbe; (δ) staphylococcus pyogenes (aureus, albus, citreus); (ϵ) two varieties of streptococci. These observations lose considerably in value from the want of evidence as to the presence and disposition of these organisms in the tissues. Chantemesse and Widal found in the walls of the intestine and in the mesenteric glands of a man who died of dysentery, and in the stools of five persons suffering from the disease, a bacillus to which they attached pathogenetic importance. It is supposed by some authors that this microbe was no other than the bacterium coli commune which had acquired special virulence; this bacillus was found in pure cultures to give rise in animals to the symptoms and lesions of dysentery. The B. coli communis, usually a harmless denizen of the intestinal canal, has been proved capable, under certain conditions, of becoming a virulent pathogenetic agent, penetrating and multiplying in the tissues, and giving rise to purulent and septic inflammation. The observations of Bertrand and Baucher suggest that this microbe can become modified in appearance as well as in character; and the frequency with which its name has lately appeared in connection with dysentery justifies our worst suspicions.

Calmette, who studied the endemic disease at Saigon, came to the conclusion that of all the bacteria found in the stools the B. pyocyaneus was the one of the greatest pathogenetic importance; and the only one, in his opinion, capable of reproducing in animals the lesions of dysentery: he adds, however, that the pathogenetic effects of this microbe are excited and reinforced by its association with streptococci.

So far from finding in amœbæ an explanation of the lesions of tropical dysentery, he speaks of them, rather incautiously, as I think, "plutôt commes des auxiliares utiles pour les cellules macrophages de l'intestin."

In the fæces of patients suffering from the chronic dysentery of warm climates, Bertrand and Baucher found practically the same organisms as those met with in the acute disease in France—"mêmes vibrions, mêmes microcoques, mêmes bactéries ou bacilles, de part et d'autre"—but they conclude that in the tropical form the B. coli communis, more or less modified, predominated. In the endemic dysentery of Egypt, along with the amœba dysenterica, Kruse and Pasquale always found streptococci and other bacilli, which "manifestly contributed to the evolution of the morbid process"; so that here at least we have to do with a mixed infection.

No recent researches have been made on the bacteriology of sporadic dysentery or of that of war. The early observations of Prior on the presence of cocci in the former, and those made by American physicians on bacilli and cocci in the tissues of the intestine, are too indefinite to be of much service.

The following conclusions and inferences appear to be justified by the facts which have been under review:—

i. The healthy intestine is capable of much resistance to the infective agents of dysentery. Many persons subjected to the causes of the disease escape; and dysentery is prevalent in communities the members of which are liable to intestinal disturbances.

ii. The healthy human being carries within him organisms capable, under certain conditions, of giving rise to inflammation of the intestinal tract; and, besides, organisms of suppuration, putrefaction, and sepsis are everywhere present which have the power of determining dysenteric inflammation in the bowel when its nutrition is impaired.

iii. A simple catarrhal condition of the bowel—which may be brought on by defects in quality or quantity of food, by impure drinking-water, by exposure to cold or heat, by malaria, or by diseases of the liver inducing persistent congestion of the portal system—is sufficient in itself to promote true dysentery. Some of the microbes usually present in the bowel as harmless parasites (notably the B. coli communis) may become virulent in catarrh of the mucosa; moreover, the loosening of the epithelium facilitates their penetration into the tissues.

iv. When we observe a body of men seized with an infectious form of dysentery immediately after being subjected to hardships and depressing meteorological influences, while another body in the vicinity, having the same food and water-supply but not subjected to the like fatigues and hardships, escape, we are led to infer that the common exciters of inflammation, rather than any specific agent, must have given rise to the disease: and this inference is strengthened by the fact that this form of dysentery may occur in countries where dysentery is least common, where the assumed specific agent is not habitually in evidence, and at seasons of the year when ordinary dysentery is seldom met with.

How far the discovery of the increasing virulence of successive inoculations may help to explain the epidemic and infective characters of this form of the disease cannot at present be determined.

v. The mode of spread of true epidemic dysentery, and certain points in the history of endemic dysentery—such as its gradual decline in certain countries, its special prevalence in others, and its endemo-epidemic manifestations—cannot at present be explained without assuming the existence of one or more infective agents which impair or destroy the vitality of the bowel, and lay it open to the attack of the organisms already existing in the fæces of dysentery.

vi. How much of tropical dysentery is caused exclusively by the amœba dysenterica is still uncertain.

MORBID ANATOMY.—I. **Acute Dysentery.**—*Seat of the Disease.*—Dysentery is essentially a disease of the large intestine; but it not infrequently invades the lower part of the ileum, as it did in the Cumberland and Westmoreland Asylum outbreak, which, it may be remarked, assumed in all instances the croupo-fibrinous form. It would be interesting to know whether this invasion of the ileum is in any way related to the form of the disease, to the media by which the infection has been conveyed, or to the port of entrance. In the instance to which I have just alluded the dysenteric agent was air-borne, and consequently must have entered through the mouth. In many cases of dysentery the lower part of the small intestine is injected in patches without any sign of ulceration. In most instances, indeed, it is remarkable how strictly the disease is limited by the ileo-cæcal valve; the upper surface of it, indeed, may be healthy, while the lower surface is the seat of inflammation and its results. Dysentery often involves the whole gut from the cæcum to the anus; but it is usually more pronounced at the cæcal or anal extremity. The dysentery contracted in the Ashanti expedition of 1874 was of a very dangerous type, and was usually associated with malarial fever. The disease, in this instance, invariably implicated the cæcum; and in three-fourths of the cases the cæcum was the part primarily and principally affected. My own experience points to the cæcum as the starting-point of that severe gangrenous form of the disease met with in tropical malarious countries. Speaking of ulcerations of the intestine in dysentery, Annesley says: "It may be stated that they are generally most remarkable, both in respect to size and numbers in the cæcum, and next so in the sigmoid flexure of the colon and rectum." Kelsch and Kiener's observations, relating to Algeria and Tunis, point to an extension of the dysenteric process from above downwards, the later but severer lesions being found in the sigmoid flexure and rectum. On the other hand, while admitting that the starting-point of the disease varies in different countries, Bérenger-Féraud's experience in the West Indies and Senegal leads him to the conclusion that "the lower end of the large intestine is really the point most frequently and profoundly attacked." From the tables given by Lyons, we judge that in the Crimea the rectum, sigmoid flexure, and descending colon were the principal points of attack; and this is in accordance with the observations of Pringle, Munro, Cleghorn, and other army surgeons who have witnessed the dysentery of war in temperate climates. Mayne and O'Brien leave us in no doubt that in the famine dysentery in Ireland the rectal end of the canal was the part most affected, the structural changes being less marked towards the cæcum. It will probably be found that the point of origin of the disease is not a matter of accident, but closely depends upon its character or associations; the gangrenous dysentery of tropical malarious countries showing a special predilection for the cæcum.

Forms of Dysentery.—Viewed from the standpoint of morbid anatomy we recognise two forms of dysentery—the *purulo-gangrenous*, and the *fibrinous or pseudo-diphtheritic.* The commonly described *catarrhal* form is to be looked upon as the initiatory stage of both varieties. The severer forms of what is called catarrhal dysentery met with in temperate climates, characterised by thickening, softening, and sloughing of the mucosa and submucosa, differ in no respect, except in intensity, from the purulo-gangrenous form so common in tropical countries.

The fibrinous form is met with indeed, but somewhat exceptionally, in the more malarial regions of the tropics. In temperate climates, on the other hand, it represents the predominating element in the severer outbreaks of true epidemic dysentery; and it occurs, as we learn from Fagge, rather frequently in the sporadic disease as is still met with in England. In the famine dysentery of Ireland in 1848-49 it was the only form observed. "The walls of the intestine," says Mayne, "were always abnormally thickened and indurated. When grasped the bowel felt semi-cartilaginous, cutting like brawn." This form, frequently assuming the characters of the croupo-fibrinous variety, was also that most frequently seen in the Crimea and in the American Civil War.

External Appearances of the Intestine.—On opening the abdomen, the bowel externally may appear healthy; more frequently, however, it presents various morbid conditions: it may be greatly distended at one part of its course, and contracted or normal in calibre in another. When the disease has its seat in the cæcum, dilatation is seldom absent; when the inferior end of the tube is affected, inflation of this part of the gut is not so frequently present. The peritoneum in certain spots, corresponding to internal lesions, may be injected, or covered with lymph; or it may be dark, black, or even perforated, with limited or diffuse peritonitis. Perforations are most common towards the rectal end of the canal. Adhesions to neighbouring viscera cannot, however, be said to be a very frequent lesion in acute dysentery.

Internal Appearances: Catarrhal Stage.—The purulo-gangrenous and the fibrinous forms alike commence with catarrhal inflammation of the intestine. Death does not occur in this stage, so that our knowledge of it is mainly derived from what is seen in cases where the disease has run on to a fatal termination in one section of the canal while in another it is only beginning. The lesions in this early stage present themselves to the naked eye as more or less extensive streaks or patches of congestion. If these congested patches are closely examined the injection will generally be found unequal; points about the size of a pin's head are seen to be of a more intense red than the rest, and mixed here and there with circumscribed ecchymotic points or larger but less definite hæmorrhages. The natural folds of the intestine, which have become more prominent, are generally most affected. Even at this early stage thickening is more or less marked; and this is the distinguishing point between dysentery in its initial stage and acute diarrhœa. The solitary follicles may or may not be enlarged. The descriptions met with in medical literature of pustulo-tubercles and excrescences, often likened to small-pox, may have reference to the varying appearances which the enlarged solitary follicles present before suppuration. Sometimes, perhaps, the descriptions are intended for the wart-like deposits presently to be mentioned as occurring in croupo-fibrinous dysentery. Abrasions of the mucosa are sometimes visible at quite an early stage of the dysenteric process.

A rare opportunity occurred to Dr. Clouston of observing the alterations of the large intestine in a woman who died after two days' illness. This is what he found: the solitary glands in the lower part of the ileum were enlarged; Peyer's patches were unaffected; the mucous membrane of the cæcum was reddened and thickened in small patches, which ran into each other like the eruption of the skin in measles. The transverse colon was mottled and thickened; the descending colon and rectum were less affected. In the rectum the mottling was mixed with small red points like a pin's head. No trace of ulceration or membranous deposit was found. In this case it is to be noticed that, although there was no ulceration, there had been copious bloody evacuations.

Microscopically, the epithelium in the catarrhal stage is usually found to have been shed, the capillaries and smaller veins are distended with blood, and there is an increase of white cells in the proper tissue of the mucosa—especially marked in the neighbourhood of the vessels. In proportion as the thickening is marked so is the submucosa the seat of vascular engorgement and round-cell infiltration. In milder cases the crypts of Lieberkühn are intact or their capillaries simply engorged; but when the disease is more severe or advanced, there may be hæmorrhagic or purulent infiltration immediately around the glands as well as into the interglandular tissue, separating, compressing, or otherwise distorting them. When the solitary follicles are enlarged, nothing more than an increase in their cellular elements is observed, together with congestion of the capillaries in the surrounding mucous membrane.

Purulo-Gangrenous Form.—There is only one step from the more advanced stages of the catarrhal to the purulent form of dysentery. The thickening of the submucosa in the latter is greater, and the muscular coat is now œdematous. This thickening is caused by sero-purulent infiltration of the deeper tissues of the bowel, and in certain places hæmorrhagic extravasations into the submucosa may have taken place. The affected patches or segments of the bowel present a variegated surface. In parts they are of a livid, in parts of a dusky-red hue, while in other parts the intestine is of a yellowish brown colour; and these varying colours shade away into each other. The surface is irregular both from the development of the rugæ and also from the unequal thickening of the submucosa. Elevations are occasionally met with which stand out in greater relief, are soft to the touch, and on incision give issue to a purulent or sanious discharge, mixed with shreds of broken-up tissue—true submucous phlegmons. When the suppuration has proceeded to destruction of the mucous membrane, we meet with tracts, more or less extensive, of a paler colour, from which project irregularly-shaped islets of the still adherent (often dead) mucosa. These islets are of various colours, from a purple-red to an ashen gray. Along with these appearances bran-like specks of necrosis, limited to the summits of the ridges or more diffused, are frequently seen. In adjoining portions of the bowel, black or ashen gray sloughs, adherent or partially detached, are found surrounded by congested and thickened mucous membrane.

When the gangrenous process predominates the mucous and submucous coats of the bowel are converted into a grayish, greenish, or black sphacelated mass. Larger or smaller portions of the bowel—most frequently the cæcal or rectal portions—are thus affected; or both extremities, or even the whole of the large intestine, may be reduced to this state of gangrene. Reddening, thickening, ulceration and sloughing are frequently found side by side or in different parts of the canal.

In the worst cases of purulent softening or gangrene it is needless to look for defined ulcers. In the less acute cases, and in those portions of the bowel where the disease has made less progress, ulcers of various size, form and arrangement are met with. One of the most common in these cases is the oval ulcer, placed transversely to the axis of the canal; this when small has a tendency to occupy the transverse folds of the membrane. Round, irregular, or sinuous ulcers, some with edges ragged and undermined, others with raised, swollen, and congested edges, are also seen. The circular ulcers vary in size from that of a sixpence to that of a crown; and by their coalescence larger ulcers are formed. Many of the larger ulcers, with an irregular outline and a soft shreddy base, are the result of the discharge of sloughs of corresponding size. Sometimes circular, sharply cut ulcers are found in the sigmoid flexure surrounded by congested tissue. Superficial ulceration of irregular form and indefinite extent is occasionally found in the reddened, velvety, thickened mucosa. When the disease has been of some standing and of a minor grade, the round, punched-out follicular ulcer comes into evidence, either isolated, or aggregated so as to give a sieve-like appearance to the mucous membrane.

As no synthesis of the lesions can give an adequate idea of their combination in individual cases, a few notes of what has been actually seen may help to give definition to the picture.

Case 1.—The mucous membrane of large intestine reddened and thickened throughout, with irregular superficial ulcerations in the descending colon and sigmoid flexure. The submucosa infiltrated with pus.

Case 2.—The whole canal from the cæcum to the anus involved. Large portions are in a state of sphacelus—black and humid. On pressure or section a putrid, offensive grumous fluid exudes. In other parts of the bowel the sloughs have separated, and no vestige of the mucosa or submucosa remains. The muscular coat is pale, swollen, and softened.

Case 3.—The cæcum externally is distended and of a dark colour; the vermiform appendix is gangrenous. The interior of the cæcum is black, with ragged shreds of sloughy tissue here and there visible, and contains a quantity of a dark-red putrid fluid. The ascending colon is thickened and reddened. One oval transverse ulcer, about an inch and a half in diameter, is placed near its cæcal extremity; several small sloughy patches of a gray colour farther on. The rest of the canal congested; a few superficial ulcers in the sigmoid flexure; the rectum much reddened and thickened.

Case 4.—Stomach, duodenum, and last foot of ileum congested. Cæcum and ascending colon covered with dark green sloughs, which have in some places separated, exposing the muscular coat. The rest of the canal congested in patches. A single circular ulcer in lower part of sigmoid flexure.

Case 5.—Cæcum thickened and congested. A slough about the size of sixpence in the ileo-cæcal fossa. The sigmoid flexure and rectum are the seat of thickening, ulceration, and gangrene. The rest of the canal in a state of mottled congestion.

Microscopically, little can be made out when the stages of purulent softening or of gangrene have been reached. When the tissues are still to some extent intact, we find the crypts of Lieberkühn bathed in pus, their epithelium detached, or their free ends destroyed; in some places they are widely separated from each other, in others compressed. The solitary glands are either loosened by suppuration or are already extruded, leaving small ulcers to mark their site; the submucosa is infiltrated with pus and blood; the connective tissue cells have disappeared or become indistinct, and the fibrous bundles opened out. The muscular coat is more or less infiltrated with pus and serum.

Fibrinous or Pseudo-Diphtheritic Dysentery.—This assumes three forms: i. We have a croupo-fibrinous deposit on the free surface of the mucous membrane, involving at the same time—to a greater or less extent—the mucosa itself. ii. A fibrinous exudation in the mucosa without any deposit on the free surface of the membrane. iii. Exudation involving the mucous and submucous coats.

i. In the first or croupo-fibrinous variety the lymphy or fibrinous deposit is of varying thickness and consistency. It is of a grayish white, greenish yellow, or rusty colour. It may cover larger or smaller portions of the bowel uninterruptedly; or it may occur interruptedly in small patches, sometimes not larger than a pea; or finally, it may appear in irregularly diffused or aggregated warty masses, some of which are not larger than a pin's head.

Microscopically, the deposit consists of an amorphous or indistinctly fibrillated material penetrating into the glands—which may thus be compressed, pushed apart, or sacculated—and involving the adenoid tissue of the mucosa. The tissue implicated in this process becomes necrosed, and is either disintegrated, or separated and thrown off by suppuration originating under the necrosed layer.

ii. The superficial non-croupous, fibrinous exudation is limited to the mucosa, without any appreciable deposit on the free surface. It appears as specks, streaks, or small patches of a yellowish brown or brick-red colour, implicating by preference the summits of the folds. The mucosa is infiltrated with granules, white cells, and red corpuscles; the submucosa is thickened, and more or less infiltrated with round cells; the blood-vessels both of the mucosa and submucosa are congested. The *eschar sec* of Kelsch and Kiener, described as "small nodosities of the size of a hemp seed to that of a pea," and ascribed by them to a coagulation-necrosis process, answers to the form now described; the conception of the nature of the lesion being the only point of difference. Indeed the coagulation-necrosis view of the process, in many cases of this variety, may well [illegible] the right one. When the necrosed tissues break down, or are thrown off, ulcers are left which often tend to burrow under the mucous membrane, extending in depth by suppuration, and superficially by coalescing with neighbouring ulcers; the intervening tissue is destroyed, as a rule, by suppuration, but sometimes, as the blood-supply is cut off by the undermining process, by sloughing.

iii. The fibrinous dyşentery, which involves at once the mucous and submucous coats of the bowel, is one of the most dangerous forms of the disease. The bowel is rigid, sometimes semi-cartilaginous, much thickened, and its calibre often correspondingly narrowed. Its internal surface is uneven and variegated in colour—yellow, green, red and black. It is firm on section, having something of the consistence and the red and yellow streaky, homogeneous appearance of bacon.

Microscopically, the exudation consists of an amorphous granular or fibrillated substance, which along with pus and red corpuscles intrudes itself between the elements of the normal tissue, and into the pathologically formed interstices. From the pressure of the exudation the glands are separated, elongated and compressed; and the connective tissue of the submucosa is broken up. Gangrene of the compressed tissues is the inevitable result of the process. A combination of the purulent and diphtheritic forms is not unusual.

Repair.—In the more extensive and destructive lesions characteristic of gangrenous dysentery, and of the secondary gangrene consequent on fibrinous exudation, repair is out of the question; yet there can be no doubt that recovery does take place after very extensive sloughing, implicating the mucous and submucous coats. Dutrouleau, for example, records an instance in which the patient recovered perfectly after discharging by stool 35 c.m. (about 13 inches) of the mucous and submucous coats. The process of repair in the bowel does not differ from that which obtains in other tissues; although here it is retarded, and the results rendered more precarious by the functional activity of the parts. In the bowel, as elsewhere, we have the development of new granulation tissue; the levelling down of the indurated, elevated edges by absorption; the depression and ingrafting of the overhanging borders of still living portions of the mucosa surrounding the ulcer. These processes suffice, when the ulcer is of moderate dimensions, to restore the continuity of the canal; and little but pigmentation remains to indicate the site of a former ulcer. When large losses of substance have resulted, the contraction of the newly-formed fibrous tissue gives rise to puckered cicatrices, and thick white fibrous bands result which, while restoring the continuity, too often diminish the calibre of the bowel and obstruct the canal. The mucosa of parts less severely involved often undergoes more or less atrophy.

II. Chronic Dysentery.—The morbid anatomy of the chronic disease reveals the results of the acute process, or appearances indicative of the supervention of an acute attack. Matting of the intestines together by lymph and adhesions to the neighbouring viscera are frequently met with. The canal at one part may feel soft, thin, and atrophied, in another doughy, in a third cartilaginous. Internally the surface is pale—often of a slate colour, or, in places where an acute process may have been in progress, red and congested. The solitary glands are frequently enlarged or pigmented. Ulceration and cicatrices are the predominating lesions. The ulcers may be small or large, few or many, elevated with indurated edges, or level with the surrounding mucous membrane. The small punched-out follicular ulcer is also met with in recent cases. Solitary ulcers of varying size are often found above constricting bands, and occasionally in other situations. Constrictions from external or internal causes are common; the latter, arising from cicatrices, are most frequent in the descending colon, sigmoid flexure, and upper part of the rectum; but they may exist in other situations.

Microscopically, we meet with new tissue elements, and with various modifications of the normal structures, such as deformation, shortening, cystic dilatations of the crypts of Lieberkühn, and their inclusion into the solitary follicles. The risk of perforation from deep-seated suppurating ulcers should not be forgotten.

Associated Pathology.—The lower part of the ileum, as we have already stated, is frequently involved in the croupo-fibrinous form of dysentery. In recent cases the small intestines are often hyperæmic in patches; in chronic dysentery the ileum is often pale and notably atrophied. The mesenteric glands are enlarged and softened; or in old-standing cases they may be indurated or pigmented. The liver may be hyperæmic, enlarged, softened, or, in chronic cases, pale and fatty: it is frequently the seat of abscess, multiple or solitary. When dysentery is associated with the malarial infection the spleen is generally large and soft; otherwise it is normal, or occasionally small.

Pneumonia is frequently, and pleurisy occasionally, a complication of dysentery. The kidneys are often found congested; especially when the liver is diseased. The peritoneal coat of the bladder is occasionally covered with lymph, and when the disease, in a severe form, is seated in the lower part of the bowel, its internal surface sometimes shows signs of increased vascularity.

SYMPTOMATOLOGY.—**I. Acute Dysentery.**—(*a*) *Simple Dysentery.*—I shall first describe the symptoms met with in the severer cases of simple dysentery, and then give an account of those proper to the gangrenous form. Simple dysentery, indeed all dysenteries, may set in suddenly after a period of constipation; but it more frequently begins as a diarrhœa which has nothing about it to excite suspicion of what is to follow. During this premonitory period some loss of appetite and general malaise may be complained of. When the looseness has continued for a day or two, griping begins to accompany the motions, which also become more frequent, and are passed with some uneasiness, increasing to straining. The stools now change their character. The fæces of the diarrhœal stage (if such existed) are first mixed with mucus streaked with blood, and then replaced by it; blood and mucus soon constitute the entire evacuation, which is preceded by more distressing griping pains (tormina), and by more prolonged and painful straining (tenesmus). The ingestion of food or drink, or movement of any kind, provokes a call to stool; but apart from any such provocation a continual desire to evacuate the bowels is present, which is but momentarily, or not at all, relieved by going to stool. Long-continued straining results in the passing of a small quantity of bloody mucus, and the smaller the quantity the greater the straining. Occasionally small, hard masses of fæces (*scybala*) are passed. After a few days the anus becomes inflamed, and is the seat of burning pain which brings on spasmodic contractions; these at a later period give place to relaxation of the sphincter ani; and prolapsus may ensue. When the rectum is deeply engaged the bladder sympathises, and dysuria increases the sufferings of the patient. Fever is frequently absent, or the rise of temperature is insignificant. It is rare that the fever in uncomplicated dysentery makes its *début* by a rigor. When the patient has suffered or is suffering from the malarial infection there is often also an evening rise of 2° or 3° F. In the more intense forms of malarial poisoning the temperature has been seen to rise to 104° F. or higher; but such temperatures are not to be looked upon as proper to dysentery. In the later stages the pulse becomes weak and fast, the appetite is impaired, and the tongue coated; and in some cases a subicteric tinge is observed. Vomiting is generally absent, and is seldom urgent, unless the dysentery is complicated with an inflammatory affection of the liver. The urea and uric acid are in excess, the chlorides diminished. Albumin, if present at all, is in small amount, unless in the severer forms of the disease. Pressure in the tract of the large intestine elicits pain, even in cases in which it is not otherwise complained of.

The stools, which in mild cases vary from 15 to 50, and in severe cases may number 150 a day, consist at first of mucus and blood. This, at least, is the case when the disease is limited or chiefly confined to the lower extremity of the bowel. After a time they assume a serous character. A reddish fluid, mixed with small flesh-like lumps—the *raclure de boyaux* of French physicians—makes its appearance. This fluid, unlike that of the first stage, is rich in albumin. The mean daily loss of albumin in a dysentery of moderate severity has been estimated by Oesterlen, as quoted by Woodward, at fifty or sixty grammes, a drain which accounts for the rapidly increasing debility of the patient. The mucous motions have a nauseating, the serous ones an offensive odour, both distinctive of the disease.

When the disease, as is often the case in the tropics, is chiefly located in the cæcum and ascending colon, the symptoms assume very different characters; and these are often overlooked in text-books. The motions are more abundant, more fæculent, and less frequent. They are preceded by griping pains, but are passed with little straining, except when the lower bowel is at the same time implicated. They are thin, pale, and frothy; one part of the same stool may be tinged bright yellow, another green; and all are mixed with blood and mucus. The cæcal region is the seat of uneasiness, generally of swelling; and pressure in the right iliac fossa gives rise to pain and tenderness. A varying degree of fever, nausea, and depression accompany this form.

b. Gangrenous Dysentery may supervene during the progress of a mild attack, or the symptoms from the commencement may have been of unusual intensity. The distinctive characters of gangrene are derived from the stools and the concomitant constitutional disorder. The stools are serous, of a dark brown colour, mixed with pus, membranous shreds, black flaky sloughs of the mucosa; or thicker, dark gray, shaggy, pus-infiltrated sloughs of the mucosa and submucosa, with a grumous deposit consisting of the débris of the disintegrated bowel mixed with blood and pus.

When we have to do with cæcal dysentery, the variegated fæculent stools of the first stage, mixed with blood and mucus, are succeeded by putrid, chocolate-looking motions; and, later, by copious reddish fluid stools giving a grumous deposit mixed with shreds and sloughs. The odour of the stools in gangrenous dysentery is so indescribably offensive as neither to be mistaken nor forgotten.

The constitutional symptoms are those of increasing prostration. The pulse is fast and weak; the tongue dry, red and glazed, or black; the urine scanty, often albuminous or even suppressed.

Towards the end, the tormina and tenesmus decrease or disappear, the motions pass involuntarily, the temperature sinks, collapse sets in, troublesome hiccup announces the end; but the mind generally remains clear till the last.

When a favourable issue from the gangrenous or simple form is in prospect, the motions become more healthy and fæculent, and less frequent; the urine is more abundant, the patient's strength and appearance improve, and the pulse, temperature, and tongue become normal.

Microscopically, the stools in the first stage consist of hyaline mucus, mixed with red and white corpuscles and epithelium from the bowel. At a later stage they are found to consist chiefly of blood and pus, with sloughs, broken-down tissue, and undigested fragments of food. The micro-organisms already enumerated will also be detected.

II. **Chronic Dysentery.**—Chronic dysentery, rarely originating in temperate climates, appears in three ways: (*a*) An acute attack, instead of ending in recovery, persists in a mitigated form. (*b*) Or after apparent recovery dysenteric symptoms of a milder but more persistent type continue. (*c*) The disease occasionally originates in a recurrent diarrhœa, which gradually assumes more and more of a dysenteric character.

Howsoever it may originate, a looseness, often alternating with constipation, and accompanied with more or less colic and straining, is characteristic of the malady. There are periods of quiescence when the motions are healthy, or comparatively so. These are succeeded by exacerbations, during which the calls to stool are frequent; the motions are watery, are mixed with blood, mucus, or pus, or with all three at once, have the true dysenteric odour, and are passed with some griping and straining.

When this condition is prolonged the health of the patient deteriorates: he becomes weak and anæmic; the appetite is bad, capricious, or ravenous, and his digestion is impaired, as is manifested by flatulence and uneasiness after meals, and by the passage of undigested food with the fæces.

When stenosis of the gut results from cicatricial contractions, the abdomen becomes tumid and tender; the feeling of distension is distressing; flatulent eructations occur; the breath acquires a fæculent odour, and the evacuations are scanty and voided with difficulty.

Towards the end the pulse fails, the tongue becomes red and glazed, vomiting and night sweats occur, œdema of the feet sets in, and the patient, after months or years of suffering, dies of exhaustion.

III. **Modified and Complicated Dysentery.**—*Malarious Dysentery.*—When associated with mild malaria, the only change to be observed in most cases of dysentery is an evening rise of temperature of from 1° to 3° F. When occurring in a patient who is labouring under an intense malarial infection dysentery usually assumes an aggravated type, affecting principally the cæcum and ascending colon, and tending to prostration and algidity. When algidity is marked the malarial element is almost always predominant. A form of dysentery attacked the fever-stricken troops in Mauritius after they had been removed to a non-malarious island off the coast. Power, who described it, says "the stools were a smoky, dark fluid, consisting of disintegrated blood and water. No sloughs until some time after the commencement of the disease, and not necessarily then. There was no trace of fæculent, or, indeed, of any solid matter. There was great depression, with a *tendency to coldness of the body*, but the mind remained quite clear. After death either total sloughing of the internal coats of the large intestine, or merely a prominent state of all the glands, was observed."

Yet another condition has been observed, associated with malaria, in which the patient is free from intestinal symptoms during the apyrexial intervals, while during the febrile paroxysms he passes large quantities of liquid blood, pure or mixed with fæces. In some instances this magma of blood and fæces was observed by Bérenger-Féraud to amount to three litres in two hours. Severe febrile and hæmorrhagic dysentery of a continued form may also complicate malaria, as Maget observed in Tonkin.

Scorbutic Dysentery is chiefly marked by its insidious onset, its dangerous character, and by the large amount of sanguineous fluid, mixed with mucus, shreds and sloughs, which is passed in the motions.

The Caribi Sickness of Guiana, known as el Bicho in Brazil, the mal de vallé in Ecuador, Bischeo in Trinidad, and which is probably similar to, if not identical with the epidemic gangrenous proctitis of Fiji, appears from time to time in destructive epidemics. Hartle describes the Bischeo of Trinidad as "ushered in by pyrexia and the most malignant concomitant symptoms of the malady, by profuse hæmorrhage from the bowels and extreme relaxation of the sphincter ani. In some of the cases the tenesmus is distressing, in others there was no pain whatever; yet in all the blood was constantly streaming from the rectum, while the anus was extremely dilated."

Arthritic Dysentery.—Arthritis, in some outbreaks of dysentery, as that at Caen in 1765, at Bloomfield in Ohio in 1851, and in Norway in 1859, is a rather frequent concomitant or sequel. The large joints are affected, especially the knees. The heart is seldom involved; and, as a rule, the disease, although tedious, is not dangerous. Those who are hereditarily disposed to rheumatism, or who have already suffered from it, are not more liable than others to be thus affected.

Septic and Pyæmic complications.—The absorption of noxious matters from the bowel occasionally produces in dysenteric patients nervous prostration, sleepiness, and low delirium. The tongue is black, the pulse feeble and fast, and the patient dies of septic intoxication. Pyæmic symptoms, with recurring chills, parotitis, diffuse abscesses, or peritonitis, are also met with occasionally in the severer forms of the disease.

Typhus and *Typhoid Fevers* are frequently associated with the dysentery of famine and war.

Liver complications.—Mild cases of dysentery generally run their course without any appreciable sign of liver complication. In the majority of the severe cases in tropical climates, however, whether terminating favourably or fatally, this organ is more or less implicated. In a considerable number of cases signs of liver-trouble precede, by some time, the intestinal disorder; in other instances the liver and bowel are simultaneously affected; while, in the majority of cases, symptoms of acute congestion of the liver, perhaps only in abeyance at first, declare themselves during the progress of the dysentery, and frequently enough after a rather sudden diminution in the number of the stools. Pain, or only a sense of weight, in the right hypochondrium, increased on deep pressure, accompanied or not by a slight rise of temperature, an enlargement of the organ, with nausea or vomiting, and frequently a certain degree of jaundice, mark the presence of a congestive liver complication. When these symptoms are followed by a rigor, or accompanied by a distinct increase of fever and hectic symptoms, the formation of an abscess may be suspected. There is an undoubted tendency to acute hyperæmia of the liver in dysentery. In some cases it would appear as if a common cause gave rise to both affections, while either appears during its progress capable of determining the other. When the liver complication arises during the course of a dysentery, we are justified in referring it to the action of poisonous materials formed in the intestinal canal and carried to the liver by the portal vein.

RELAPSES AND SEQUELS.—**Relapses** are liable to occur after exposure to cold and indiscretions in diet, and are more commonly observed in persons enfeebled by the abuse of alcohol.

Sequels are seldom observed after mild seizures. After more severe attacks paralysis, reflex or neuritic in origin, of the lower extremities, of the sphincter ani, and of the bladder have been observed. Troubles of digestion, hepatic disorders, hæmorrhoids, prolapsus ani, irritation of the bladder, cystitis, and œdema of the lower extremities may also be reckoned amongst the sequels of the disease—disorders of the digestive functions being the most common.

DIAGNOSIS AND PROGNOSIS.—A careful study of the symptoms of the disease, along with an inspection of the stools and an examination of the abdomen (which should never be omitted in these cases), will suffice to guide the practitioner to a correct diagnosis. The prognosis must depend partly upon the nature of the epidemy, or of the prevailing type of the disease; mainly on the character of the stools, their frequency, the presence or absence of sloughs or of a gangrenous odour; upon the presence or absence of fever or of liver abscess, and, finally, upon the extent to which the constitution is affected by the local disease. Hiccup, when it occurs in the later stages, great nervous prostration, low delirium, a decrease of the tormina accompanied by increasing debility and inflation of the abdomen, and algidity are all of evil import.

PROPHYLAXIS.—The prophylaxis of dysentery must be deduced from its etiology. The resident in countries where the disease is endemic or epidemic should see that the soil in the neighbourhood of his dwelling is not subjected to fæcal pollution. He should make sure of the purity of his water-supply; and if there be the slightest reason for suspicion on this score the water should always be boiled before use. This is a precaution that should never be neglected by travellers in tropical regions, where all water should be looked upon as suspect, and treated accordingly. Food should also be of good quality, well cooked, and excess and defect alike avoided: alcoholic stimulants, if used at all, should be taken in strictest moderation. Diarrhœa and constipation alike should be guarded against.

Exposure to wet and cold must be avoided as far as practicable. When the clothes get wet, whether by perspiration or rain, they should be changed as soon as possible. The cummerband, or abdominal belt of flannel, should be used in the tropics. Dysenteric stools should be disinfected and disposed of by covering them deeply with earth at a distance from the dwelling. In camps they should be disinfected immediately and then disposed of by cremation. Bed-pans, commodes, clyster-pipes, and bedding should be thoroughly disinfected. Redoubled attention to these precautions are to be enforced when the disease is epidemic. The prophylaxis of war and famine dysentery is an important matter of state policy; and demands the prevention and avoidance of the remoter causes of the disease.

TREATMENT.—Experience has confirmed, what reason teaches, that one kind of treatment does not answer in all forms of dysentery, nor will one drug suit all stages of the disease. Dr. Clouston, in the outbreak of the croupo-fibrinous dysentery already referred to, tells us that he tried the ipecacuanha treatment in every possible way—by mouth and rectum, in doses from ten grains to a drachm, alone and in combination with opium—without success. In the malarious dysentery which attacked the troops in Mauritius, ipecacuanha was found to be of no service; but the disease seemed to yield to large doses of the tincture of the perchloride of iron. The form of dysentery that attacked the inmates of Millbank Penitentiary in 1823-24 resisted blisters, bleeding, fomentations, and the train of astringents, bitters, aromatics, and ipecacuanha, which were tried in succession. The one remedy that proved of real value was mercury, in the form of gray powder or calomel, which, as Latham says, was given at first with the greatest apprehension after all other medical expedients had failed. In some cases in which the agony from tormina and tenesmus was extreme, and the evacuations enormously frequent, and consisting altogether of blood or morbid secretions, fifteen grains of calomel and two grains of opium were given, and afforded marked relief. Mayne also states that he and his colleagues found mercury to be "the principal remedy" in the famine dysentery which prevailed in the South Dublin Union Workhouse in 1848-49. Among more recent authorities, Trousseau and Bérenger-Féraud—the experience of the former being limited to France, that of the latter to the French tropical colonies—attest the value of this remedy in some severe forms of the disease. Niemeyer considers the administration every two hours of one grain of calomel, with quarter of a grain of opium, to be the "most trustworthy treatment" in the higher grades of dysentery. I give these experiences somewhat in detail, because I am about to recommend a different treatment, warranted by my own experience and that of others in tropical countries. But if it be true, as I believe it to be, that more than one morbid state is included under the name of dysentery, we shall be prepared to find that the treatment adapted to one form may not be useful in another. The physician, therefore, should not allow doctrinal prejudices to prevent him from having resort to remedies which have been found life-saving in certain forms of the malady.

The chief point, however, in all forms of dysentery alike, is the hygienic and dietetic treatment, and many of the milder cases yield to this alone. Rest is, in this disease, an important curative agent. The patient should be put to bed at once. As Celsus says, "Oportet in primis conquiescere, siquidem omnis agitatio exulcerat." The room should, for obvious reasons, be well aired and free from draughts.

In many cases the patient will feel relief from the application of a linseed-meal poultice, large enough to cover the whole abdomen, both belly and sides, and changed before—not after—it begins to get cool: care must be taken, in the act of changing, that the patient is not exposed to cold, and that the bed-clothes are protected from damp. If there be considerable gastric irritation, a sinapism, or spongio-piline placed in hot water and sprinkled with turpentine, will be of service. Cases occur in tropical countries in which the patient, suffering from fever and drenched in perspiration, finds that poultices add to his sufferings: under such circumstances they are to be avoided. A warm bath given, with due precautions, at the very beginning of the disease, is often useful. As the anus is apt to become excoriated, the physician must see that the orifice is washed with tepid water containing some disinfectant after each stool. A warmed night-pan should be used to prevent the patient getting out of bed.

The diet is the next point, and, I need not say, an important one in a disease in which the food-canal itself is affected. In most instances the patient should be restricted to a milk diet, pure and simple; condensed milk will answer if perfectly fresh milk of good quality cannot be obtained. Milk diet is as advantageous in the chronic as in the acute stage; and is especially valuable when there is a scorbutic tendency. The milk may be given pure, or diluted with lime water, and is administered in the intervals between the doses of medicine. For the first few days, unless the patient be in a low state, he should not be urged to take nourishment oftener or more largely than he desires; and in all cases the needs and feelings of the individual should receive due consideration. When pure milk is not well supported it should be given with full doses of pepsine; or peptonised milk may be substituted.

While, in most cases, milk is the best diet for the dysenteric patient, it should not be held as a doctrine that in milk, and in milk alone, there is safety. Sometimes it is not obtainable, and occasionally it is not well supported by the patient, in any form. In these exceptional cases strong beef essence, made from a pound of good meat minced, mixed well in a mortar with two ounces of water, transferred in an hour to a properly secured jar, placed in a vessel of boiling water for three hours and strained, should be given in doses of a table-spoonful frequently. Along with it whey may be given as a drink if the patient be thirsty. When prostration is great, not otherwise, wine or brandy is indicated. Clouston found that the administration of liquid nourishment, and of wine and water at will, was the only treatment that he was quite sure did good.

In most uncomplicated cases of tropical dysentery the ipecacuanha treatment should be adopted; and I believe that this treatment is also the best for the catarrhal stage of dysentery in temperate climates. It seldom fails when given from the onset of the malady. When the disease has been preceded by constipation, a preliminary dose of sulphate of sodium or calomel should be given to carry off fæcal accumulations. If, on the other hand, there is no reason to suspect such retention, twenty to thirty grains of ipecacuanha powder made into a bolus should be given at once, and the dose repeated every six, eight, or twelve hours, according to the urgency of the symptoms and the tolerance of the remedy, until a fæculent motion is obtained. If the first dose cause vomiting, this will do good rather than harm; but the second dose should be preceded by a sinapism placed over the pit of the stomach, and twenty to thirty drops of laudanum (for an adult patient) should be given half an hour before the second dose, and no liquid taken for two hours before the bolus is administered. With these precautions the second dose is seldom rejected. It is better, as a rule, to rely upon the ipecacuanha alone; but in some instances, when the tormina are very distressing and the calls to stool excessively frequent, from ten to fifteen minims of laudanum may advantageously be added to each bolus. The intervals between the doses should be sedulously utilised for the administration of nourishment.

The first sign of improvement is the passage of a fæculent stool, after which the tormina and tenesmus decrease. The treatment as directed should be maintained for some time after signs of amendment have appeared; but when the disease has assumed the characters of a simple diarrhœa, salicylate of bismuth, alone or combined with Dover's powder, will usually prove sufficient to check the looseness, if careful attention to diet be continued.

De-emetinised ipecacuanha, first recommended by Surgeon-Major Harris, has been employed of late years in the treatment of dysentery. The conflicting estimates of the therapeutic value of this substance are largely owing to its varying composition. Some of these preparations, which contain little of the extractive matters soluble in alcohol, are inert; others, retaining the greater part of these extractives and sometimes an appreciable residue of emetine, have been given with success, in doses of twenty to thirty grains, at intervals of six to twelve hours. Prof. Notter informs me that de-emetinised ipecacuanha has been tried in the chronic forms of dysentery which come so frequently to Netley, "but the experience here recorded is that in such cases its properties are inferior to the ordinary ipecacuanha." Until a wider experience has determined the value of this substance, I strongly advise the use of the ordinary drug. The nauseating and even the emetic properties of ipecacuanha, in moderation, are beneficial; they produce a sedative effect on the circulation; and determine a free action of the skin with consequent relief to the portal system, which materially contributes to the cure; especially in acute cases with fever, or with congestion of the liver. The de-emetinised drug may be employed with advantage in mild cases, in those in which the prostration is extreme, and in the rare instances in which ipecacuanha in its natural state gives rise to uncontrollable vomiting.

When there is much dysuria a hypodermic injection of morphine may be resorted to; but in this complication a warm bath is often beneficial, and if not otherwise contra-indicated should be tried.

When the disease is very acute, confined to the lower part of the bowel, is still in the stage of mucous evacuations, and the patient robust, much relief will be obtained from the application of a dozen leeches around the anus.

This treatment by large doses of ipecacuanha has proved so successful that it should not on light grounds be set aside in favour of any other. If for any reason it should be inadmissible, the saline treatment, so much and so successfully used in France, may be resorted to. The sulphate of sodium is the salt generally employed, and is given in solution in doses of one ounce to an ounce and a quarter, in the morning. Its purgative action commences from one to four hours after ingestion, and ceases in ten or twelve hours. The dose should then be repeated unless the urgent need for rest require delay. It was remarked by Trousseau that the cure is the more certain the greater the number of the evacuations: still there is no use in urging purgation beyond a reasonable limit; and half an ounce of the salt four times daily will generally suffice in mild cases.

The sulphate of magnesium, with the addition of dilute sulphuric acid in doses to act gently on the bowels, has proved efficient in the dysentery of Bengal.

The constant presence in the stools of organisms that undoubtedly exercise a destructive influence on the tissues of the intestine, and, by means of the poisonous materials they generate, frequently cause disease of the liver, and occasionally of the kidneys, suggests to us a resort to antiseptic remedies by the mouth or rectum in all cases of dysentery, as auxiliary to the ipecacuanha treatment. Experience, so far as it goes, is in favour of attempting to produce antisepsis of the intestinal canal by the administration of antiseptic remedies by the mouth; and, as these need not interfere with the treatment either by ipecacuanha or salines, there is no reason why so hopeful a method should not be adopted. Benzo-naphthol is the remedy to be preferred whenever there is a suspicion of liver or kidney complication; and when no such complications exist, it is as effective as any intestinal antiseptic at present in use. Forty to eighty grains may be given during the twenty-four hours, in divided doses every two, three, or four hours, in the intervals between the other remedies.

Beta-naphthol and resorcin are also employed as intestinal antiseptics, and may be substituted for benzo-naphthol when this is not at hand—thirty to fifty grains per diem of either, in divided doses, being given every three or four hours. Perhaps somewhat larger doses than these may be tolerated and required. Benzo-naphthol and beta-naphthol, being insoluble, must be given in capsules, or dissolved in oil and emulsified. Resorcin is soluble, and can be readily administered in any aqueous vehicle. The solubility of resorcin and the readiness with which it is absorbed in the stomach and upper part of the canal rather detracts from its value in dysentery when administered by the mouth.

Ipecacuanha and the salines act as intestinal evacuants. They clear, or wash out, so to speak, the intestinal canal, helping to remove, at the same time, the microbes and toxins which may be present. But when the rectal extremity of the bowel is the sole or chief seat of the disease, the use of enemas especially—mild, non-irritating, antiseptic injections—responds to the causal indication. In cæcal dysentery, on the other hand, we cannot carry out disinfection by enema with safety. Enemas are not indeed so useful in practice as we might suppose. When the disease has reached the stage of suppuration, ulceration, or gangrene—when antiseptics are most required—the bowel is so disorganised and friable that the use of large enemas is not devoid of danger, and small ones fail to cover the entire area of the disease. Frequently also the anus and rectum are intolerant of the introduction of the clyster-pipe. It is in the earliest stage, before the integrity of the bowel has been seriously impaired, that good is to be expected of large enemas. The colon of an adult has a capacity of three to four pints; a large enema may be taken to mean from one and a half to two and a half pints.

A large tepid water enema is often useful at the beginning of the disease; and may be made antiseptic in some measure by the addition of boracic acid, benzoate of sodium, or resorcin. If it be repeated small doses of the antiseptic should be added at first, and the increase of the active ingredient regulated by the observed effects and the susceptibility of the individual patient. Our experience of antiseptics in dysentery, especially in the way of clysters at the early stages, is still rather slight; but given by mouth and rectum they furnish resources that may hereafter enable us not only to treat cases successfully which resist other remedies, but may materially diminish the risk of hepatic complications, and reduce the number of cases that become chronic.

In some instances, in which the ipecacuanha treatment has failed, and the symptoms become more and more aggravated, threatening to end in gangrene, pills containing one grain of calomel, two grains of ipecacuanha, and a quarter of a grain of opium have proved useful. The pills should be repeated every hour at first, until five or six have been taken; and then every two hours during the day, and less frequently at night. The medicine should be continued until an improvement in the stools appears, but should not be carried to salivation. When the stools have changed, ipecacuanha is to be resorted to again in order to complete the cure. It sometimes seemed to me that ipecacuanha most frequently failed in the diphtheritic forms, and that in these mercury succeeded.

One of the most dangerous forms of the disease is that which I have designated *cæcal dysentery*—a form which, in the tropics, is often associated with a severe type of malarial fever. In this form prostration at an early stage is often so great that ipecacuanha is contra-indicated. The de-emetinised preparation may be tolerated, and deserves to be tried in these cases. Quinine in full doses, with milk or essence of beef and frequent small doses of wine, is, however, our first resort. If a purgative be indicated, thirty minims of turpentine with the smallest purgative dose of castor oil should be given; and this should be followed by ten-minim doses of turpentine in mucilage every two or three hours. If the kidney be diseased, benzo-naphthol should always be substituted for turpentine; and in all cases an attempt should be made to promote antisepsis by this substance. Turpentine stupes applied over the cæcum, or over the abdomen generally, may also be used.

Should algidity manifest itself, warm applications to the extremities, stimulants internally, in small and repeated doses, and subcutaneous injections of ether are indicated.

In the *hæmorrhagic form associated with malaria*, quinine and the tincture of the perchloride of iron are to be given—the latter tentatively. Matico infusion by mouth and rectum was found serviceable in the malignant hæmorrhagic dysentery occurring in Trinidad, already mentioned under the name Bischeo. The value of ergotin, in hypodermic injection, should not be overlooked if there be reason to suppose that an eroded vessel is the source of the hæmorrhage.

In the *scorbutic* form, in addition to the regulation of the diet—which should include the use of lemons, limes, oranges, or grapes—fresh bael fruit has been strongly recommended. Maclean found it most useful when given in the form of a sherbet. When the motions contain much dark and liquid blood, fifteen to thirty minims of oil of turpentine in almond emulsion will often act like a charm. When turpentine is contra-indicated, as in kidney disease, a solution of one of the astringent salts of iron may be used. It may be as well to mention that there is a dysenteric scorbutus as well as a scorbutic dysentery, the drain on the system causing scorbutic spots. In this form the stoppage of the drain is the primary indication. *Arthritis* appearing in the course of dysentery demands only the use of local applications. When symptoms of *liver congestion* appear in the early stages of tropical dysentery, as they frequently do, intestinal antisepsis should be the more sedulously employed; but this complication should in no way be allowed to interfere with the administration of ipecacuanha, which acts favourably on liver and bowels alike. When abscess is actually present, the saline treatment, already explained, should at once be substituted.

Treatment of Chronic Dysentery.—Chronic dysentery occurring in European residents in tropical countries demands a change to a temperate climate. Minute directions as to the precautions necessary to avoid or mitigate the possible dangers of such a change should be given. If the voyage has to be undertaken in winter a short stay on the Riviera may be advisable. The patient should wear a flannel belt sufficiently wide to cover the whole abdominal region. The sea-voyage itself is often beneficial when the arrangements on board for invalids are good; and such a voyage may be recommended with advantage in the case of those who cannot afford the time and expense involved in a prolonged stay in Europe. Warm clothing, avoidance of draughts, careful regulation of diet, and change to a temperate climate should be looked upon as the most important measures in the treatment of this disease.

During exacerbations the diet must be restricted to milk, the patient kept in bed, and the treatment adapted to the acute disease; modified, however, according to the urgency of the symptoms. The disease is a protracted one; and this has to be taken into account in regulating treatment, diet and exercise: the patient is weak; nourishing, easily digested food is therefore essential. When walking is unadvisable or impossible, carriage exercise is to be taken as frequently as the weather and the state of the patient permit.

The whole course of the large intestine should be carefully explored in order to detect swelling, hardness or tenderness. From a careful consideration of the results so obtained, and of the character of the stools, an effort should be made to arrive at a probable estimate of the existence, or otherwise, of cicatrices, ulcers, and tracts of congestion.

When the existence of ulceration is inferred, constipation must be obviated by the gentlest laxatives, and diarrhœa checked by the guarded use of the mildest astringents, accompanied, if gastric or intestinal fermentations be suspected, by the antiseptics. When cicatricial contractions in the lower part of the bowel interfere with its evacuation, emollient and antiseptic enemas may give relief. In chronic ulceration, especially when seated in the lower part of the bowel, enemas of nitrate of silver have frequently proved beneficial, but I have never seen good follow the heroic use of this remedy. A wet compress to the abdomen is not only grateful to the patient, but often has a remedial influence on the congested bowel.

Warm baths, gentle laxatives, frictions to the abdomen, and emollient, laxative, and antiseptic enemas must be our chief resort in those hopeless cases in which stenosis is established. It is remarkable how many apparently hopeless cases do improve, how many even recover perfect health; but while this should encourage us not to despair, the distressing helplessness of the physician in presence of the aggravated forms of chronic dysentery should lead us, by greater attention in the treatment of the primary disorder, to render the chronic form of less and less frequent occurrence.

ANDREW DAVIDSON.

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A. D.

BERIBERI[1]

Synonyms.—*Barbiers, kakke,* etc.

Definition.—A specific endemo-epidemic form of multiple peripheral neuritis which, in addition to the usual phenomena of that condition, is characterised by special liability to implication of the phrenic and pneumogastric nerves—the cranial nerves as a group and the higher nerve centres being practically exempt; and, also, by a marked liability to varying degrees of œdema of the connective tissue, and of effusion into the serous sacs of the thorax and abdomen. The infective agent, as yet unknown, is not obviously communicable from person to person directly, but it can nevertheless be carried from one place to another; it clings to particular localities, buildings, and ships; it requires for its pathological manifestation moisture and a high atmospheric temperature, and it is particularly operative under conditions of imperfect ventilation, overcrowding and defective dietary.

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[1] The local names for beriberi are infinite. In Java it is known by the natives as *Loempoe;* in Banka as *Pantjakit niloe*, or *siloe* (crystal sickness), *Binas, Apooi;* in New Guinea as *Pantjakit papoea;* among the Malays as *Kaki lem but* (weak legs); in the French Antilles as *Maladie des sucreries;* in Cuba as *Hinchazon* (dropsy) *de los negros y Chinos;* in Brazil as *Perneiras* (ailing feet); in Matto-Grosso as *Inchcão;* in Ceylon it was at one time known as *the bad sickness of Ceylon.* In Japan it is sometimes called *Ashike;* the term most commonly used there, however, is *Kakke*, a word which is now very frequently used by European writers. It is well to remember that the term "kakke" is strictly synonymous with beriberi, and does not indicate a special Japanese form of the disease, as some seem to suppose.

There has been much useless and inconclusive discussion about the etymology of the word beriberi—the name officially recognised by the College of Physicians of London. All that is with certainty known is that the word is of Eastern origin. The attempts which have been made to settle its etymology amount to little more than ingenious speculation. Meyer-Ahrens derives it from the Hindustani *beri*, a sheep, in allusion to the peculiar gait in some instances of the disease; Platteeuw derives it from the Sudanese *biribi, biribit, berebet*, stiff walking, pottering walking; Marshall from the Singhalese *bharyee*, weak movement; Herklots from the Hindustani *bharbari*, swelling, œdema; and Carter from the Arabic *buhr*, asthma, and *bahri*, a sailor, in allusion to the fact that it is a form of dyspnœa frequently met with among sailors in the Arabian seas. Simon says that during a visit paid to Ceylon he definitely ascertained that "beriberi" is a Singhalese word, which simply means "a very bad sickness."

Certain medical writers, dissatisfied with the somewhat uncouth term beriberi, have suggested various Latin or Greek names, most of them referring either to the dropsical or to the paralytic phases of the disease, or indicating some theory of its nature which may or may not be correct. Thus we have *Hydrops asthmaticus* (Rogers), *Synclonus beriberia* (Mason Good), *Myelopathia tropica scorbutica* (van Overbeek de Meijer), *Neuritis multiplex endemica* (Scheube), *Paraplegia mephitica* (Swaving), *Sero-phthisis perniciosa endemica* (Wernich) *Panneuritis endemica* (Bälz).

History.—There can be no question of the extreme antiquity of beriberi. Strabo and Dion Cassius contain passages referring to it, or to a very similar disease which broke out in the Roman army invading Arabia in 24 B.C. Chinese writers so early as the second century of our era make distinct allusion to it. According to Macgowan, it is mentioned in the *Neiching*, the oldest medical treatise extant, and attributed to Hwang-ti (B.C. 2697). It is also mentioned in Japanese books of the ninth century A.D.; but Scheube, who has devoted much attention to the literary as well as to the scientific aspects of beriberi, thinks that the allusions were borrowed from Chinese works; and he concludes, from the evidence of contemporary writings, that the disease appeared in Japan for the first time about the middle of last century. Although in the earlier modern European works—from Bontius onwards—relating to Eastern diseases, beriberi was distinctly recognised, and, so far as the knowledge of the times permitted, accurately described; latterly the subject seemed for a time somehow to have dropped out of the medical literature, particularly the English medical literature, of tropical disease. Indeed, there was a tendency among authors to deny its existence as a specific disease, and to relegate it to some such category as anæmia, scorbutus, malaria, or rheumatism. But the recrudescence of the disease in Brazil about 1863, the opening up of Japan to foreign intercourse and the discovery that the "kakke" of that country was none other than the beriberi of the Indies, the epidemics in the Singapore jail and in the plantations of the Malay Peninsula and Archipelago, and the ravages of the disease among the Dutch troops in Atcheen, have in recent years concurred to force it again into notice.

Perhaps recent advances in neuro-pathology, the discovery that what were formerly regarded as ill-defined and unclassified groups of palsies are attributable to inflammation or degeneration of the peripheral nerves, and that these pathological conditions in their turn are attributable to certain poisons, have done more than anything else to forward the study and knowledge of beriberi; for it has been clearly proved by Scheube and Bälz in Japan, and, later, by Pekelharing and Winkler in the Netherlands Indies, that beriberi is, in fact, a specific form of peripheral neuritis; and this opinion is now generally accepted. Until this generalisation was made, the symptoms and their singular grouping had received no satisfactory explanation.

At the present time investigators are attempting to advance yet one step further. They are busily endeavouring to find the beriberi poison itself, which may be either a micro-organism, or a chemical substance the product of such a body.

Geographical Distribution.—Although cases of beriberi have been reported as far north as the island of Saghalien, and although I have known the disease to originate in the port of London in the crews of ships which had been in harbour for several months, its geographical limits may be practically stated as being about 45° N. (the island of Yesso), and about 35° S. (the city and neighbourhood of Monte Video). Commencing at the eastern coast of Asia, beriberi occurs in Japan as far north as Hakodadi, being very common in the large towns of the empire, such as Tokio, Yokohama and Kioto, especially in houses situated in the low damp districts. In Corea it is said to be prevalent, particularly on the south-east coast. I have met with no account of its occurrence in China to the north of the Yangtse River; but at Shanghai, and at all the treaty ports south of that city, in Formosa, and in Hong-Kong it is often met with. It has also been reported as endemic at Fatshan, a city a considerable distance up the Canton River; how much farther the disease extends into the interior of the Chinese Empire is not known. It was epidemic in Manila in 1882-1883, and appears to prevail there at the present time. It has also been reported from Tonkin and from Cochin-China. In Singapore, Malacca, Penang, and in the surrounding country, and in many other places in the Malay Peninsula, it occurs with great frequency. It is even more common in Java, Borneo, Sumatra, and in many of the islands of the Eastern Archipelago, the warm, damp atmosphere of which seems particularly suited for its development. Thus in Atcheen it has proved a scourge to the Dutch troops, native and European, and to their camp-followers. It is perhaps the most serious difficulty planters and miners in the Malay country have to contend with. Every year thousands of their coolies succumb to this disease; in some localities the mortality from this cause is appalling—over 50 per cent. Beriberi has been seen in Australia, usually as a ship disease or in imported cases: recently Wetherall reports an epidemic among sixty aboriginals who had been imprisoned at Kimberley, Western Australia (11), and Corlette and Molloy describe outbreaks among the Chinese in Sydney and Melbourne. The disease at one time seems to have been common enough in India; if it is rarer in recent years, this is possibly due to better barracks and improved hygiene in jails, schools, and large public institutions generally; not to the absence of the disease among the native population. Recently we have accounts of outbreaks in Burma as high up the Irawaddy as Mandalay. According to Giles the disease popularly known in Assam as "beriberi" is really ankylostomiasis. Although Kynsey entertains a similar view as to the nature of the beriberi of Ceylon, there can be little doubt that genuine beriberi is to be met with in that island now as formerly. The disease known as *epidemic dropsy*, which visited Calcutta and neighbourhood, and Mauritius also, in 1877-1880, and which has been described by some as beriberi, although in certain respects resembling this disease, appears to me to have shown many differences,—chief among which were the low mortality, the invariable presence of extensive dropsy, the short duration of the attack (three to six weeks), the absence of pronounced anæsthesia and paralysis, and the frequency of an eruption. [*Vide* art. on "Ep. Dropsy," p. 475.] True beriberi does occur, however, in Mauritius and in the neighbouring island of Bourbon, where the chronic atrophic forms formerly had the name of "barbiers." It also occurs in Madagascar, Zanzibar, and probably elsewhere on the east coast of Africa. It has often been met with on the west coast of that continent; lately it caused a terrible mortality among the coloured labourers on the Congo railway. In America beriberi has been reported from Cuba, Guadaloupe, Panama, Venezuela, and Cayenne. Of late years it has been extensively prevalent in Brazil and in Uruguay, and has been encountered as far south as Monte Video. It is said to occur in the Sandwich Islands, but we have little information on this point either as regards these islands or the islands of the South Pacific. Beriberi, if it occur at all, is certainly rare in Europe. It is just possible, however, that some of the obscure cases of peripheral neuritis that crop up from time to time are of this nature; when peripheral neuritis occurs in epidemic form, as in the outbreak at the Richmond Asylum, Dublin, in 1894, most probably it is beriberic in nature.

As a general rule in the countries mentioned beriberi is found principally in the low-lying districts along the coast and on the banks of rivers; at the same time, provided they supply the necessary conditions of heat and moisture, mountainous districts and table-lands are not exempt. Thus, according to Bälz, beriberi occurs at Shinano in Japan at an elevation of 800 metres above the sea-level. In the endemic areas it everywhere shows a marked preference for the low-lying quarters of cities; for barracks, forts, hospitals, schools, jails, mines, coolie lines on plantations, and for all limited spaces wherein large numbers are crowded together.

In endeavouring to fix the geographical distribution of beriberi it must be borne in mind that our knowledge of the diseases of the natives of many of the countries within the limits indicated is very defective; that, as a matter of fact, it is only at a few trading centres, for the most part on the coast-lines, that we have an opportunity of learning anything about such matters; and that even at these points, owing to absence of suitable hospitals, ignorance of native languages, and disinclination on the part of the people to consult European physicians, investigation has been very imperfectly conducted. Important diseases, even great epidemics, may exist among the natives of the interior, and even of the coast, and yet the Europeans settled among them may remain in complete ignorance of the fact.

A remarkable feature about beriberi is its tendency to occur in ships. In the early days of European trade with the East, when ships were small and crews were large, when voyages were protracted, and when the forecastle was crowded with ill-fed, poorly-clothed native sailors often accompanied by their families, beriberi frequently broke out among them; although, as was often noted, it rarely spread aft to the officers or European quartermasters. Even nowadays beriberi is far from being uncommon among the native crews of steamers trading to the East. The Seamen's Hospital at Greenwich is seldom without examples of the disease landed from these steamers. Not many years ago beriberi was so common in the Japanese navy that one-fourth part of the service was annually attacked. Similarly a large percentage of the natives and a few of the Europeans in the Dutch men-of-war in the East Indies suffer from the disease—more formerly than at the present day. Another curious fact in its connection with ships is that, like yellow fever, it seems to cling to particular ships, and to reappear in their crews year after year. I once observed this in the case of a Chinese gunboat in which, though scrupulously clean and well found, cases of beriberi cropped up annually over a number of years, appearing regularly among the crew soon after the setting in of the hot weather.

Symptoms.—Before an attack of beriberi fully declares itself there is usually, though not always, a premonitory stage of longer or shorter duration. For several days, or perhaps weeks, the patient feels languid, is easily fatigued and put out of breath, is depressed in spirits, and has feelings of numbness, stiffness, or even cramps in the legs, which may be tottery and feeble; headache is not uncommon; there may be some form of catarrhal trouble, such as diarrhœa; or there may be occasional transient flashes of fever, or what seems to be an attack of malarial fever. Some days the patient may feel comparatively well and fit for work, on other days he is languid and lies up. He may notice that his ankles are slightly œdematous, and perhaps that his face has a puffy look.

With or without such a premonitory stage, symptoms of pronounced peripheral neuritis are slowly or rapidly evolved. During several days the symptoms are gradually intensified; or, it may be, the patient, who had gone to bed the previous evening in apparently fair health, finds on waking next morning that he is hardly able to walk or even to stand; his shins and finger-tips are numb, his calf muscles are tender, and he is conscious of a variety of paræsthesiæ—such as burning and tingling—in feet, legs, and arms; his ankles and shins are swollen, and his hands and face puffy. By slow degrees, or rapidly, these symptoms are aggravated, the œdema becomes general, the paresis of the legs becomes almost complete, the arms become weak, and the hand-grasp enfeebled. Palpitations and breathlessness, with substernal and epigastric distress, recur in paroxysms at longer or shorter intervals, and the urine becomes reduced to a few ounces. This condition may be further aggravated by cramps in the calf muscles, which now feel stiff, full, and exquisitely tender when pressed or squeezed. The knee-jerks cannot be elicited.

In this state of œdema, of partial paralysis, of muscular hyperæsthesia, of cutaneous anæsthesia and paræsthesia, of breathlessness, of palpitation, of substernal and epigastric distress and oppression, the patient may remain for several days, several weeks, or even for a month or two. His appetite is not materially impaired; he finds, however, that indulgence in a full meal increases the epigastric disease, and so, as a rule, he eats somewhat sparingly. Digestion is fairly well performed and the bowels are regular—if anything inclined to constipation. His intellect is in no way disturbed, and, as a rule, he has no fever. He converses freely, and, unless when troubled with cramps, myalgic pains, palpitations, or dyspnœa, his state is by no means an uncomfortable one.

After a variable time, during which he has ups and downs, he begins to pass urine more freely; coincidently with this, the œdema begins to subside. And now, when the œdema has almost disappeared, it is discovered that the muscles of the legs and arms have undergone a high degree of atrophy. Very often the atrophy progresses to such an extent that the whilom muscular coolie is reduced almost to a skeleton. He lies in his bed quite unable to move, or he may just be able to creep slowly about with the aid of a stick, or by clinging to the furniture and walls for support. He has no knee-jerk, he cannot stand with his eyes shut, his muscles are still very sensitive to pressure, the skin over the shins and the finger-tips is still numb, he buttons his clothes with difficulty, and he walks, if walk he can, like one struck with locomotor ataxy.

Then comes a long period of weeks or months during which the muscles are slowly restored, the hand-grasp gradually returns, the power of locomotion slowly improves; last of all the knee-jerk reappears, but this may not be for very many months, perhaps for a year or more.

Such is a brief description of an ordinary and uncomplicated attack of beriberi of average severity. There is a moderate amount of œdema, a moderate amount of anæsthesia, of hyperæsthesia of muscles, of paresis. There are occasional attacks of palpitation and of epigastric oppression. After a time, as the œdema subsides, evidence of extensive muscular atrophy is disclosed, and during a prolonged convalescence the wasted muscles are slowly restored.

But such a description by no means applies to all cases. During an epidemic, and constantly in the endemic regions, every imaginable variety and modification of the essential symptoms, both as regards intensity and combination, are encountered. Thus the œdema may in one case be so insignificant as to be barely detectable, and that only over the crests of the tibias or about the ankles. In another case it may be excessive, involving trunk and limbs and face, so that the patient looks as if he suffered from acute nephritis. Often in such a case the muscular paresis is really but slight, the principal hindrance to movement being the dropsy. Again, the brunt of the disease may fall on the muscles, which rapidly waste; the patient in a few weeks, with scarcely any accompanying œdema or but a mere trace over the tibia, being rapidly reduced to a skeleton, paralysed in legs and arms, perhaps unable to move hands and feet, or even fingers or toes. In a third case the most urgent and striking symptoms may be referable to implication of the pneumogastric and phrenic nerves; when cardiac oppression, palpitation, dyspnœa and substernal pain are the prominent features. In yet another though much rarer variety the prominent symptoms may be such as are produced by pericardial or pleural effusions. Again, many cases are encountered in which for a few weeks there may be some muscular weakness about the legs, some numbness and slight œdema over the shins, perhaps slight numbness of the finger-tips; but the symptoms are so trifling that they do not interfere with the patient moving about and doing his work as usual, and the threatening signs gradually subside without culminating in an attack of well-marked neuritis. On the other hand, cases are met with now and again in which the symptoms develop so rapidly that almost before there is time for a diagnosis the patient is *in extremis* from cardiac or diaphragmatic and intercostal paralysis, and may die within twenty-four hours from the beginning of the attack.

In view of this great variety of form various classifications have been attempted. When œdema is the most prominent symptom the case is designated *wet* or *dropsical beriberi*, sometimes *beriberia hydrops.* When paralysis and muscular atrophy are the prominent features, the case is called *dry, paralytic* or *atrophic beriberi*, sometimes *beriberia atrophia.* Where the case is marked by a moderate amount of œdema, and a moderate amount of paralysis, it is sometimes called *mixed beriberi.* Where the cardiac and respiratory symptoms are very urgent, develop rapidly, and quickly terminate in death, the form is called *pernicious.* The adjectives *larval* and *rudimentary* are sometimes applied to the cases, above referred to, in which the symptoms are of a trifling and unimportant character. The terms *acute, chronic, relapsing, recurring* are used occasionally to indicate rapidity, or slowness, or recurrence of the disease.

It must be borne in mind, however, when using any of these terms that they indicate only phases of the same disease, and not different diseases; and also that the various phases are not sharply marked off one from another, but that they graduate insensibly into each other; and, moreover, that one form may rapidly assume the characteristics of another form—the hydropic become the atrophic, the atrophic become the hydropic, the chronic acquire acute features, and all or any of them rapidly assume a pernicious character.

In proceeding with a somewhat more detailed account of the symptoms of beriberi, we note, first, that there is no evidence of an unquestionable character that any of the higher nerve centres are ever attacked directly. The mental faculties are not markedly affected until perhaps the patient is dying; neither, unless very exceptionally, is there any implication of the centres or nerves of sight, hearing, smell, or taste; nor, with the exception of wasting of the subcutaneous fat in certain cases, and some rare forms of erythematous eruptions in others, is there any evidence of such trophic lesions of the integuments as we are accustomed to associate with spinal disease. Bed-sores, for example, are not met with in uncomplicated beriberi. Scheube records a case of what may have been trophic joint lesion; but such cases are extremely rare.

The lesions of beriberi are, all of them, such as we are accustomed to associate with disease of the peripheral nervous system. Essentially they are of the same class, and many of them identical with those found in alcoholic, diphtheritic, and the other forms of neuritis. Just as there is a tendency for each of these specific forms of peripheral neuritis to display a more or less characteristic grouping of symptoms peculiar to itself, and just as the poison of each of these diseases shows a predilection for particular sets of nerves, so beriberic neuritis, whilst it presents many features in common with the other forms of peripheral neuritis, presents special features more or less distinctive and peculiar to itself.

Fever.—It is by no means established that fever is in any way an essential feature in the history of beriberi, although at one time or another in the course of many of the cases it may occur. Sometimes beriberi supervenes on what may or may not have been a malarial attack, or develops in the course of such an attack; at other times fever, which may or may not have the characters of a malarial attack, may come on soon after or long after well-marked beriberi is established. I have observed in cases of beriberi, in which these intercurrent attacks of fever were a feature, that the symptoms of neuritis were aggravated after the febrile attacks, as if these attacks depended on and were symptomatic of the exacerbations of the neuritis. In chronic cases there is no fever, or only as a coincidence; in many such cases temperature is probably subnormal, as it certainly is in all cases in which cyanosis is present and death approaches.

Œdema.—The extreme liability to œdema is one of the peculiarities of beriberic neuritis: a comparatively rare thing in other forms of peripheral neuritis, in every well-marked attack of beriberi it is an invariable feature, either throughout or at one time or another. It invariably commences in the lower extremities, usually over the crest of the tibia—over its inner surface, and about the ankles. It may be trifling in amount and confined to these regions; on the other hand, it very often extends to the dorsums of the feet, and, spreading upwards, gradually or quickly involves thighs, trunk, face, and upper extremities, sometimes attaining an extreme degree. Moderate œdema, besides its invariable situation on the shins, is usually best marked about the flanks, the root of the neck, and over the sternum. The degree of swelling may vary from day to day. To the touch the œdema feels rather firmer than the œdema associated with kidney disease, pitting less readily. It differs in another respect from the latter and from cardiac œdema, inasmuch as it does not usually involve the genitals to a great extent. A peculiar localised œdema is sometimes met with, especially about the hands and arms. In this a limited and sharply-defined area of integument, some four or five inches or more in diameter, is puffed out to a great extent. These localised swellings may develop in the course of a few hours, and disappear as suddenly. In some cases the œdema precedes by a few days the paresis and anæsthesia.

Urine.—The occurrence of a high degree of œdema is always coincident with a diminution in the quantity of urine voided and with a rise in its specific gravity. But although there is a rise in the specific gravity of the urine, this rise is not proportionate to the diminished amount of fluid excreted by the kidneys. The total solids are considerably below normal: according to Scheube the chlorides are proportionately less than the urea. Especially is this the case when there are extensive serous effusions; and on resorption taking place the urinary solids reappear in proportionately larger quantities. According to the same authority the excretion of phosphates is increased; and, according to Bälz, indican is abnormally abundant. The quantity of the urine may be reduced to a few ounces; in rare instances the secretion is entirely suppressed. Although it occasionally contains albumin, this is an accidental and not a common feature. With an active diuresis the œdema may entirely disappear in a day or two.

Anæsthesia.—The anæsthesia varies in extent and degree between very wide limits. In the great majority of cases, like the œdema, it is an early symptom, and, as a rule, is best marked and appears earliest over the front and inner aspect of the legs. In mild, and sometimes even in severe cases, it may not extend beyond this. Usually, however, it creeps downwards over the dorsums and perhaps the soles of the feet, and upwards over the thighs; particularly on their inner and anterior surfaces. It spares the groins, perineum and genitals. At an early stage it appears on the inner surface of the wrists, the backs of the hands, the fingers, finger-tips and palms, attacking them in the order stated. It may creep up the inner surface and back of the arm and involve the elbow. In many cases the skin over the chest and abdomen is also affected. Observers in Japan agree in describing a circle of anæsthesia around the mouth. This has not been noted so distinctly elsewhere.

The anæsthesia usually amounts merely to a blunting of sensibility and a delay in perception. The patient when touched feels as if a glove or piece of cloth were interposed; on testing with an æsthesiometer the tactile areas are found to be enlarged. In rare cases the anæsthesia is complete. The perception of chemical, electrical, thermic and painful stimulus is also diminished and delayed in the implicated areas. It is further to be noted that the patches of anæsthesia are not in conformity with the anatomical distribution of particular nerves; that, though usually symmetrical, in rare cases the anæsthesia may be limited to one side of the body; that in certain cases the finger-tips are the parts first or most involved; that the degree of anæsthesia varies from time to time in the same case; that it is worst in atrophic beriberi; and that its degree and extent are not always proportioned to the gravity of the case.

Hyperæsthesia of the skin has been noted (Scheube); it is a very unusual condition.

Paræsthesias—such as burning, pricking, formication, gnawing, darting pains, coldness, a feeling as if the affected part were swollen—may precede or accompany the other symptoms and prove very distressing.

Paresis to a greater or less extent always affects the muscles of the legs, and very often those of the arms and hands; less frequently those of the trunk and face; very rarely those of the eye; and still more rarely the sterno-mastoid, the trapezius, and the muscles of mastication and deglutition. As a rule, the muscles supplied by the peroneal and anterior tibial nerves are those first affected, then—and for the most part in the order mentioned—those of the calf, the extensors of the knee, the glutei, the flexors of the knee, the adductors and flexors of the thigh. Usually, coincidently with the appearance of paresis in the thigh, the muscles of the forearms and arms are attacked, including the extensors of the wrist and fingers, the supinator longus, the triceps, the flexors, and the small muscles of the hands and fingers. Then the abdominal muscles, the pectorals, the intercostals, the laryngeal muscles, and the diaphragm may all, one after another, become affected. The heart, too, as shown by subjective symptoms, is very generally more or less implicated. The muscular structure of this organ, when carefully examined, has invariably been found affected.

The power of locomotion is impaired conformably with the degree of paresis. In beriberi of a mild type the patient can walk with or even without the aid of a stick; the legs may feel a little weak and tottery, but the hands and arms are hardly at all affected, and the patient can therefore steady himself with a stick or otherwise. In a more severe form locomotion is difficult and clumsy. Generally in such a case the hand-grasp and finger power are decidedly impaired. In cases of yet greater severity, not only is locomotion impossible, but practically all movement is in abeyance, except perhaps those of facial expression and the movements of the eyes, and those associated with speech, mastication, deglutition, and respiration; and not only is the paralysis of the limbs complete, but that of the trunk is equally profound. In such a case coughing may hardly be possible owing to paralysis of the larynx and the muscles of forced expiration; and speech may be reduced to a whisper. In all such cases the feet fall into the equino-varus position in line with the legs, and the hands drop at the wrists. The patient is quite unable to feed himself, perhaps quite unable to make the slightest movement; he simply lies on his back atrophied and helpless.

Many writers allude to a *beriberi gait* as if it were something peculiar. There is nothing so peculiar in it, however, to distinguish it from the gait of similar forms of peripheral neuritis. In walking, because of the paralysis of the flexors of the foot, the toes tend to brush the ground on the attempt to raise and advance the foot. This is a very usual condition in the milder forms of the disease. In more severe cases, in which the extensors of the foot as well as the flexors of the leg and thigh are also engaged, the heel can no longer be raised. Consequently, if walking be still possible, it will be found to have degenerated into a sort of shuffle—more of a swing forwards of one side of the body with the corresponding leg, first of one side then of the other, than a walk. In bad cases the patients have recourse to a variety of contrivances to facilitate locomotion. As already mentioned, some help themselves along by clinging to the furniture; others—their legs well apart—lean with both hands on a stout stick which is thrust out well in front of them, and to which, while leaning their weight on it, they drag themselves as it were; some patients, still retaining considerable power in their arms, but completely paralysed in their legs and quite unable to stand, by placing their hands on the ground behind them and sitting half up, contrive in this attitude to push themselves along.

Few beriberic patients can stand for any length of time with eyes shut or even with feet closely approximated. They sway and would fall like an ataxic patient. Doubtless imperfect perception of the ground, as well as muscular weakness, has something to do with this; and, very probably, there may often be in addition an element of incoördination.

The hands and arms exhibit similar muscular incapacity, though, as a rule, in a relatively slighter degree. Thus the weakening of the finger muscles, together with the blunting of sensation in the finger-tips, and perhaps slight incoördination, may render buttoning and unbuttoning of the clothes a difficult or even an impossible task. Writing and similar delicate movements may also be impossible. The hand-grasp is in most cases decidedly weakened; in severe cases, as already mentioned, wrist-drop is pronounced.

When the abdominal and perineal muscles are seriously implicated, on an attempt to cough, the unsupported diaphragm is forced down and the front wall of the belly shot forwards, the perineum being manifestly bulged downwards at the same time. In such circumstances one can understand that defecation and micturition may be seriously interfered with. The sphincters are not affected.

During recovery a spastic-like movement of the muscles—particularly of the legs—is sometimes remarked. Occasionally, as a sequel of the muscular degeneration, permanent weakening of the foot flexors occurs; and, perhaps, as a result of a contraction of the gastrocnemii, organic and permanent retraction of the heels may result.

Hyperæsthesia of the affected muscles is always present, sometimes in a very high degree, so that if any of them be compressed between the fingers, or pressed against underlying bone, the patient suffers considerable pain, sometimes so severe as to cause him to cry out; such pressure is in certain cases intolerable. This symptom is most easily elicited in the gastrocnemii, in the thenar muscles, and in those of the forearm, and is of much practical use in diagnosis.

Cramps are common, especially at the outset. They may come on spontaneously at any time, but are most frequent during the night or on movement. The muscles in rare cases may be thrown into a state of tetanic contraction. A convulsive form of beriberi has been described. Opisthotonos has also been observed.

Atrophy, as a rule, rapidly supervenes in the paretic, hyperæsthetic, usually flaccid muscles. This atrophy is generally very evident on the subsidence of the œdema in hydropic beriberi, and almost from the outset in the atrophic form. The wasting is often extreme. Restoration is but slowly effected, many months elapsing before the process is complete. Occasionally one or more muscles are permanently atrophied.

Swelling of the muscles has sometimes been observed: in these cases the bellies and outlines of the muscles are prominent, and the patient, though excessively feeble, may have the appearance of an athlete. This condition appears, in most instances, to depend on œdema in the connective tissue of the muscles; in a few cases, possibly, on vascular congestion. Circumscribed swellings are not infrequent in some of the muscles, particularly in the inner belly of the gastrocnemii; their exact nature has not been determined.

The reaction of degeneration can be demonstrated throughout the disease; as Pekelharing and Winkler point out, changes in the electrical reactions can be demonstrated even before any other symptom of impending beriberi has shown itself.

Tenderness of superficial nerve-trunks can sometimes be elicited.

The patellar tendon reflex is generally in abeyance. In a few cases it is said to be exaggerated, in others to be normal.

The superficial reflexes are usually preserved; but they, too, in high degrees of atrophic beriberi are also for a time abolished.

Inflammatory swelling of the lymphatic glands of the groin, according to Scheube and others, occasionally occurs; and, according to Bentley, *congestion of the fauces*—sometimes very intense—is an almost invariable condition in beriberi.

The blood is said to be defective in alkalinity; but this statement, like many others regarding the chemical alterations in the blood, must be taken with caution. Many careful and reliable estimations of the corpuscular richness and of the hæmoglobin of the blood have been made; the opinion of all the later observers is that although beriberi may be accompanied by anæmia, and may cause anæmia, it is by no means the result of anæmia, as was at one time supposed. In a large proportion of beriberic cases, indeed, the corpuscular richness of the blood is perfectly normal. As a producer of anæmia the beriberi poison is infinitely weaker than that of malaria or even of rheumatism.

The pulse, usually accelerated, is exceedingly sensitive to exertion, even to change of posture. Scheube remarks that in bad cases slowing of the pulse may occur before death. He refers to two cases; in one of these the pulse fell in five days from 120 to 54, in the other from 104 to 20. The finger and sphygmograph indicate the condition of the circulation as characterised by relaxed arterial blood-pressure and diminished heart power.

Bruits, usually systolic in rhythm, are present in a large proportion of cases; occasionally there is accentuation, more rarely, *reduplication* of the second pulmonary sound. Some observers have noted reduplication of the first sound at the apex. *Pulsation in the veins of the neck* is also common, and is probably the result of tricuspid insufficiency from dilated right heart.

Palpitation is often the most troublesome of all the symptoms. It is provoked by exercise, by eating, sometimes even by rising up in bed: sometimes it is persistently present. It is usually worst at night, or in the morning; and is often accompanied by dyspnœa or apnœa. Often there is epigastric pulsation. Cardiac oppression is often a very urgent subjective phenomenon, and may occur independently of palpitation. Frequently also there is a feeling of fulness amounting to pain in the region of the stomach, which is possibly connected with the heart or with some condition of the diaphragm.

Enlargement of the heart to the right, as indicated by percussion and diffusion of impulse, is often very evident, and may be associated with extreme dyspnœa, cyanosis, and other indications of failing heart power.

Aphonia and *vomiting* unconnected with digestion indicate implication of the pneumogastric, and are always, particularly the latter symptom, regarded as of grave import.

Diaphragmatic and intercostal paralysis is not uncommon.

Serous effusion into the pericardium is by no means an uncommon condition, but it is somewhat rare for the effusion to be so extensive as to amount in itself to a danger.

Hydrothorax also occurs, but as a grave complication from its amount it is even rarer than hydropericardium: *ascites*, to a notable extent, is rarer than either.

Œdema of the lungs is very apt to occur in the hydropic form of beriberi, and is frequently the immediate cause of death. Its occurrence is indicated by increasing dyspnœa accompanied by cough and frothy expectoration, and, if the patient live long enough, by fine moist crepitations.

Digestion is usually feeble. A full meal may cause distress from cardiac pressure; rice is said to be ill borne, and probably for this reason.

Diarrhœa is not uncommon at the outset; at a later stage constipation is often a marked feature in hydropic beriberi.

Mode of Death in Beriberi.—In the progress of a case of beriberi, no matter how trifling it may appear, and particularly if the patient remain under the conditions in which the disease was contracted, symptoms indicating great danger may set in suddenly and at any moment. This may be within a day or two of the outset of the attack, or it may not be for one, two or more months. The threatening symptoms for the most part appear to depend on extension of disease to the pneumogastric or phrenic nerves, on the occurrence of œdema of the lungs, on the development of extensive hydropericardium, or, it may be, on a combination of one or more of these conditions. In the great majority of cases, however, the principal factor in the fatal event is the paretic condition of the right side of the heart; when this is marked, a very slight increase of other unfavourable conditions may turn the scale and bring about fatal overdistension. In rare cases death may occur from sudden syncope; usually, however, it is the result of the slower distension process. As this advances, the patient is seized from time to time with agonising dyspnœa; he sits up in bed struggling for breath, his face is cyanosed, his eyeballs start out of his head, and his cervical vessels pulsate visibly. The heart's impulse is diffused, and is communicated to the epigastrium. Percussion shows that the right auricle and ventricle are dilated, and loud bruits indicate that the valves are incompetent. The extremities become blue and cold, the temperature falls, cyanosis deepens, the patient becomes unconscious, and after a short time dies. If he recover from one such attack the chances are that another and more severe one will supervene in a short time; and sooner or later one of these attacks will prove fatal.

Mortality.—The mortality in beriberi is difficult to state; much depends on the circumstances under which the disease occurs, the opportunities there may be for removing the patient from the influences of the endemic centre, and the degree of virulence of particular epidemics. Speaking roughly, it may be anything between 1 in 40 (Japanese Navy, 1878-84) to 1 in 2 (Bahia, 1867). In many places—certain districts of Japan, for example—where the poison appears to be attenuated, and the disease to prevail in a mild form, amounting to little more than slight œdema of legs and ankles, slight numbness and feebleness of the lower extremities, with perhaps some breathlessness, the risk to life is small. In other places, however, where the poison is more virulent, graver forms of the disease predominate, and the mortality is quite on a par with that of cholera. The mortality is always specially high where the patients continue to live under the same conditions and in the same place as that in which the disease was contracted. Recently I had a conversation on the subject of the mortality from beriberi on plantations with a gentleman who at one time was medical officer on certain tobacco plantations in an important English settlement in the Malay Archipelago. This gentleman stated that the planters considered themselves lucky if at the end of a year three or four survived out of every hundred Chinese coolies imported as labourers at the beginning of the year. This terrible mortality was in great measure attributable, he said, to beriberi. The coolies were not sent away to a healthier locality when they became affected, but remained on the spot and under those influences which engendered the disease in the first instance, and which were undoubtedly equally operative throughout the continuance of the illness; thus a fatal issue was rendered almost inevitable. It appears to be with beriberi very much as with malarial disease in this respect.

Speaking generally, the nearer the equator the worse are the cases, the more numerous the hydropic forms, and the greater the mortality.

Pathological Anatomy.—In hydropic cases particularly, but also, though to a much smaller degree, in atrophic cases, there is general serous infiltration of all the tissues and a special liability to serous accumulations in the pericardium, pleuras and peritoneum, more particularly in the first. Punctate ecchymoses under the serous coats of the viscera, doubtless produced in the death struggle, are common. Not rarely larger intramuscular hæmorrhages, and similar but smaller effusions into the sheaths of the nerves, are met with. The blood is unusually fluid and dark, escaping in quantities on section of the veins, especially from those of the lungs, which are often œdematous. The brain and spinal cord, though frequently congested (particularly the meninges of the latter), are healthy, with a slight exception to be mentioned presently. There is no characteristic lesion of any of the abdominal viscera.

The special lesions of beriberi are to be found in the peripheral nerves and in the striped muscles, including the heart. The condition of the nerves has been carefully studied by Bälz, Scheube, Pekelharing and Winkler, and others. Most of these observers are agreed that evidences of nerve degeneration are always to be discovered in beriberi, that such evidences are to be found in the nerves indicated by the clinical symptoms during life, that the degeneration is most marked at the peripheral distribution of these nerves, and that it diminishes in intensity as they are traced towards the cord. They also affirm that the signs of degeneration never enter the anterior roots, and but slightly and rarely affect the posterior. In the prolongation of the latter in the cord, Pekelharing and Winkler in one case found a diminution of the number of fibres, without increase of nuclei, and without swelling or evidences of secondary changes. Scheube also found in the dorsal region of the cord of one of the six cases he examined so carefully, a diminution in the number and an atrophy of the ganglion cells in the gray matter; in the case of the anterior external group of cells this loss and atrophy he estimated to amount to one-half.

In the peripheral nerves, and most markedly in motor nerves, during the earlier stages of the disease the medullary sheath of the fibres is found to be thrown into irregular bulgings and constrictions, showing here and there (in osmic acid preparations) round black globules. In a more advanced stage the medullary sheath crumbles into smaller, irregular, roundish particles and gradually disappears, its place being taken by an irregularly disposed detritus containing large, irregular, oval, granular cells; finally the sheath of Schwann collapses, and this detritus is absorbed. At the same time the axis cylinder breaks down into irregular lengths, and it in its turn is absorbed, so that ultimately all that remains of the nerve fibre is the collapsed sheath of Schwann. The nuclei of the epineurium are not increased at the earlier stages, but later they are abnormally numerous. In time young nerve fibres, thin and pale in colour, appear to be developed. It is now seen that the nerve bundles are traversed by connective tissue trabeculæ, some of the strands being very thick: the nerve is thereby partitioned into a number of areas, many of which contain only one or two nerve fibres. These appearances Pekelharing and Winkler regard as purely the result of a degenerative process. Other observers, particularly Scheube, maintain that the initial lesion is a veritable inflammation of the nerves; they base this opinion on the hyperplasia of the connective tissue and the well-marked accumulation of nuclei in the neighbourhood of the vessels.

The changes just described have been found not only in the nerves of the limbs, but also in the pneumogastric and phrenic nerves, in the laryngeal branches of the former, and in the nerves of the heart. According to Pekelharing and Winkler, the sympathetic fibres, so numerous in the pneumogastric, show, by their finely granular appearance and the proliferation of their nuclei, evidence of implication. Similar appearances have been noted by Scheube in the renal sympathetic.

In beriberic cases the affected muscles are usually sodden and pale; occasionally in the atrophic forms they are dry and shining. In both forms the individual muscular fibres are the subject of granular or vitreous degeneration. Striation is feebly marked or absent, the fibres being much wasted or reduced to sarcolemma only. An increase of nuclei, together with overgrowth of interfascicular connective tissue, is also to be observed, particularly along the course of vessels. Young muscular fibres, or what are presumed to be such, distinguishable by their clear striation, are often visible among the degenerated fibres. Evidences of degeneration of the muscular structure of the heart, varying very much in amount, are always to be found, and here and there among the bundles points of inflammatory infiltration may be detected with the microscope. The cavities of the heart are always dilated, particularly those of the right side. Besides being dilated the heart is also hypertrophied to some extent, especially the left side.

Etiology.—Beriberi has been attributed to a multitude of different causes. Some of these—nephritis, for example—are so manifestly unconnected with the disease that it is unnecessary to discuss them. The following, however, may be enumerated—malaria, scorbutus, improper diet, anæmia, intestinal parasites, bacteria, protozoa.

There are several circumstances connected with beriberi which give a certain amount of colour to the opinion of those who have attributed this disease to malaria—meaning by "malaria" Laveran's parasite. Both malaria and beriberi are emphatically miasmatic and place diseases; both occur in limited foci where they are endemic and exhibit a tendency from time to time to spread and to become epidemic; both are favoured by heat and moisture; both affect especially those who sleep near to or on the ground; the germ of both seems capable of being wafted a short distance by the wind from the spot in which it was originally generated; in neither instance is there good reason to think that the disease is directly communicable from the sick to the healthy, but there is a certain amount of evidence that virgin soil may be inoculated, as it were, with their germs. To this extent beriberi resembles malaria.

There are so many points of difference, however, in the clinical and pathological features of the two diseases, as well as in their respective geographical distributions, that, although frequently concurring in the same locality, sometimes in the same individual—as may dysentery and malaria—the great bulk of the evidence is distinctly against their etiological identity. In beriberi, fever is not a prominent symptom; there is no pronounced periodicity in the procession of the symptoms; there is no marked tendency to enlargement of the spleen; no profound and rapidly induced anæmia; no melanæmia; no pigmentation of viscera and vessels; no Laveran's bodies in the blood; no specific relation to quinine. As regards geographical distribution it may be noted that there are many instances of malarial foci which are not beriberi foci; and also that there are a few instances of beriberi foci which are not markedly malarial. For example, Singapore is not markedly malarial, and yet beriberi is a distinct feature in many parts of it. Weintraub refers to two small forts in Analaboe,.in one of which—near the sea—beriberi is endemic, but there is no malaria; in the other—two kilometres inland—malaria is endemic, but beriberi never originates. I have often seen beriberi appear in the centre of the most populous part of the city of Victoria, Hong-Kong; in a part where malarial fevers rarely if ever originate: although such fevers are very common and malignant in the suburbs. Again, beriberi often originates in ships miles and months away from the land; well-authenticated examples of genuine malarial fevers originating under such circumstances are rare, if not absolutely unknown. It would seem, therefore, that although the germ of malaria requires for its nidus a soil composed of mineral as well as of organic matter, the germ of beriberi can vegetate on wood, and perhaps on a variety of substances into the composition of which earth does not enter.

Neither are there any better grounds for attributing beriberi to scorbutus. Beriberi occurs, it is true, on board ship; but it is found in ships in harbour as well as in ships at sea. I have seen cases of the disease from ships that had been lying for months in the port of London; I have also seen in China cases in well-found ships employed in coasting, and, therefore, constantly in and out of harbour, and abundantly supplied with fresh provisions. Formerly cases of scurvy were exceedingly common in the Seamen's Hospital, Greenwich; now they are so rare that months pass without an admission: nevertheless cases of beriberi are nearly always to be found in the wards. Were the two diseases etiologically identical we should expect to find their respective clinical symptoms frequently concurring, if not in the same individual, at all events in the same epidemic; which is certainly very far from being generally the case. Clinically the diseases are most unlike. There are no hæmorrhages, no extensive intramuscular or subperiosteal effusions, no spongy gums in berberi; in scurvy there is no evidence of peripheral neuritis.

The conjecture that beriberi originates in an unwholesome diet is founded principally on observations made in Japan. Up to 1883 the number of cases occurring annually in the Japanese navy amounted in number, on an average, to considerably over one-fourth of the muster of the entire fleet. In 1883 there were 1236 cases of beriberi in a force of 5349 men. In 1884 the dietary was changed, a larger proportion of nitrogenous food being introduced: forthwith the health of the fleet improved. In 1885 there were only forty-one cases of beriberi; in 1886 only three cases; in 1887 there was no case: and ever since, although the fleet has been very much increased, there has been a practical immunity from the disease. In 1889, in a force of 12,223 men, there was only one case. Takaki, who brought about this very great improvement, naturally regards these results as a proof of the correctness of his expressed opinions on the dietetic nature and origin of beriberi. Some support is given to this view by similar but more limited experiences—such as that of the Cossack Pearling fleet in Torres Straits. On one occasion beriberi broke out among the crews of this fleet, but was speedily checked on their receiving a supply of flour from a passing vessel; till then they had been living principally on deteriorated rice. Encouraged by these experiences the authorities, some years ago, instituted certain reforms in the dietary of the prisoners in Singapore jail, where berberi was epidemic at the time. It was believed at first that these dietetic reforms were attended with good results; but Dr. Max Simon states that later experience in the native hospitals has not been so satisfactory, and that improved dietary does not seem to diminish the mortality—at all events of the established disease, whatever effect it may have as a prophylactic. It is quite probable, nay likely, that an unphysiological dietary may cause a disposition to beriberi; but without a specific element in addition it certainly cannot of itself cause beriberi: otherwise this disease would be more or less pandemic, and not, as now, very often limited to particular districts and even to particular buildings. It is reasonable to believe that the remarkable improvement in the health of the Japanese navy, just described, was attributable partly, perhaps, to the prophylactic influence of the improved dietary, but principally to other hygienic measures introduced at the same time, and operating more directly on the germ of the disease itself.

The doctrine that beriberi is caused by anæmia is, or rather was founded on imperfect observation and limited clinical experience. Numerous hæmacytometric observations, now on record, completely dispose of this speculation. They show that anæmia, if it occur, is a consequence, not a cause of beriberi. It is a well-known fact in Japan that the rosy-faced countryman or sailor, on coming into an epidemic area, is even more liable to beriberi than the anæmic townsman.

Erni in Sumatra, and Kynsey in Ceylon, remarking the great frequency of intestinal parasites—particularly of ankylostoma duodenale and trichocephalus dispar—in beriberi cadavers, gave it as their opinion that beriberi was caused by these parasites—presumably regarding the beriberi as the consequence of an anæmia brought about by the parasites. Extended and more careful observation has not borne out this view. These parasites are very common in most tropical countries, in the sick and in the healthy alike; they do not seem to be more common in beriberic than in nonberiberic cases. Trichocephalus dispar may be dismissed at once as a cause of this disease; it is a cosmopolitan parasite—nearly as common in Russia and North Germany where beriberi is absolutely unknown, as in Sumatra and Ceylon where beriberi is endemic. A similar argument may be advanced against the claims of ankylostoma duodenale. It, too, is common in many countries where beriberi is unknown—in Egypt and in

Italy, for example. Nor in cases of beriberi in which ankylostoma is found is the number of parasites in proportion to the severity of the symptoms, or correlated in any way with them. Often in Japan this parasite is completely absent in beriberi cadavers; thus Scheube found it only once in five dissections there. Like testimony comes from the Straits Settlements and from Burma.

Bacteriology.—The best known and most important researches into this side of the etiology of beriberi are those conducted by Pekelharing and Winkler in Java and Sumatra, and continued in Europe, on behalf of the Netherlands Government. These savants assert that various bacteria—varieties of one polymorphic bacterium, it may be—are present and can be demonstrated in the blood in beriberi so long as the patient remains in the beriberi district; and that in a short time after departure from that district these bacteria disappear from the blood. They also assert that in particular beriberi districts—such as Atcheen, in which many of their investigations were conducted—such bacteria are present in the blood of all who have resided there for any length of time; in the beriberic and in the non-beriberic alike. They also state that in many of the residents in these districts palpitations, feelings of weight in the legs, and such symptoms of incipient peripheral neuritis as pains in the legs, diminished tactile sensibility of the pretibial skin area, and also slight degrees of pretibial œdema, are very common without necessarily proceeding to pronounced beriberi. They evidently regard these symptoms as akin to beriberi, and correlated with the presence of the aforementioned bacteria in the blood. They made many attempts to cultivate these bacteria, both cocci and bacilli, but with very partial success. However, in a proportion of their culture tubes they succeeded in growing a white micrococcus which, on being repeatedly injected into rabbits in large doses, at last gave rise to symptoms resembling those of beriberi; and, further, that the same micrococcus was recovered from the tissues of the inoculated animals, cultivated anew, and on reinjection again gave rise to peripheral neuritis. Similar pathogenetic bacteria they claim to have separated from the atmosphere of berberi-infected buildings.

If these observations of Pekelharing and Winkler are borne out—which to some extent they apparently have been by van Eecke, and by Mosso and Morelli—they must be regarded as being of the very first importance in settling the etiology and nature of this disease. Unfortunately Eykman and Meudes working on the same lines have failed to confirm them; and very grave objections to their validity have been advanced by such authors as Fiebig and Scheube. It has been pointed out that there is considerable probability that Pekelharing and Winkler worked with impure cultures; that their white coccus, which on its introduction was frequently followed by abscess, was the staphylococcus pyogenes albus; that neural degeneration, such as Pekelharing and Winkler describe in their experimental animals, is a common occurrence in healthy rabbits and probably in other animals, and in their experiments probably arose quite independent of their injections. The most that can be said, then, of the elaborate work of the Dutch pathologists is that it is suggestive; it is certainly far from being conclusive.

Besides Pekelharing and Winkler other observers claim to have discovered special micro-organisms in beriberi; the objections advanced to Pekelharing and Winkler's work apply even more emphatically to the other reputed discoveries.

Some time ago Glogner said he had found an organism—a hæmamœba like that of malaria—inhabiting the blood corpuscles in beriberi, which he regarded as the specific cause of this disease. Quite recently Glogner has abandoned this position.

Although it is evident from the foregoing that the question of the immediate cause of beriberi is still open, we do know something at least of its remoter antecedents. The chief of these are heat and damp—conditions which naturally obtain in many tropical climates; and even in cooler latitudes exist more or less artificially in ships and buildings where large numbers are crowded together. A combination of these conditions, overcrowding in a damp tropical climate, constitutes the ideal opportunity for the explosion of an epidemic of beriberi. The beriberi of the tobacco and other plantations in the Malay countries, the beriberi occurring in the overheated, overcrowded forecastles of ships even in temperate climates, the epidemic, already alluded to, which broke out in the Richmond Lunatic Asylum, Dublin, under circumstances of excessive overcrowding—1500 lunatics being lodged in accommodation planned for 1000, and the numerous epidemics in jails, schools and similar institutions in the tropics, may be cited to illustrate such various conditions.

There is good reason for thinking that the actual cause of beriberi is a germ or the product of a germ; but whether this germ distils its nerve toxin in the human body, or whether this toxin is a product of a germ-induced fermentation in the soil or other medium external to the human body, it is as yet impossible to say. That the beriberi germ is an organism which can multiply, and can be transferred from one place to another and there, like the malaria germ, multiply afresh, may be considered as almost established.

There are well-authenticated instances of such apparent transportation of the hypothetical beriberi germ from an infected to an uninfected place, and of its subsequent multiplication in the new locality. It would be interesting to know whether, apart from such an introduction, this microbe is ever an indigenous and normal inhabitant of the soil, and capable of permanently maintaining itself therein in the same way as the malaria microbe. The marked liability of coolies to the disease on certain newly-opened plantations in jungle lands suggests that such is probably the case.

Closely allied to this question is that of the direct *infection* of the healthy by the sick. In favour of infection is the fact that beriberi has sometimes been observed to spread to a slight extent in hospitals, even to attack successive occupants of the same bed; this I have myself observed.

Such occurrences are, of course, explicable on the hypothesis of place infection; and against direct infection there is the additional fact that the physicians and attendants of beriberi patients are not attacked. If beriberi is infectious in the same sense as are scarlet fever and small-pox, it must be to a much smaller extent.

Age has a marked influence on the disease; children under 10, and adults over 50 or 60, are rarely attacked. The most susceptible age is between 15 and 40.

Sex.—Although the data are somewhat incomplete and contradictory on the point, men are generally said to be more liable to beriberi than women. Judging from the experience of schools this rule probably does not apply to children under puberty. Parturient women, on the other hand, are especially prone to beriberi.

Occupation.—Indoor occupations, such as that of the shopkeeper and the student, and occupations implying much standing in water, such as mining, are favourable to the development of the disease.

Race.—This has probably no influence one way or another, further than that the superior hygienic conditions of the European in tropical climates imply a less frequent and less intense exposure to the specific cause than is the case with the coloured native. The European enjoys no absolute immunity; under suitable conditions he contracts the disease readily enough.

Previous attacks have a powerful influence in causation: in Scheube's cases 42 per cent were relapses; he refers to one case in which there were no fewer than twenty-four relapses.

The influence of defective diet has already been discussed. As *accessory causes* may be mentioned sudden falls of temperature, particularly if accompanied by damp; exposure to cold; fatigue; attacks of malarial fever; diarrhœa; dysentery; sleeping on the ground; surgical operations; accidents; shock; acute disease; and probably wasting diseases such as phthisis. These things seem to determine the explosion of beriberi very much in the same way as they do an attack of delirium tremens in the toper.

Acclimatisation seems to have some protective influence; nevertheless it has been remarked that the native of a beriberi district, who in his own country may have enjoyed immunity from the disease, on entering another beriberi district may be attacked. The Malay rarely gets beriberi in his own home, although the immigrant Chinese are sickening all around him; but the same Malay contracts it readily enough on board ship, or on migrating to another district. Analogous facts have often been remarked in connection with malaria and yellow fever.

The incubation period of beriberi is usually stated in months, and for the most part this appears to be so far correct. There are several instances on record, however, in which the period could not have exceeded a month or six weeks. It is well known that it is the comparatively recent immigrant who is most liable to attack in beriberi districts.

Sequels.—As can be readily understood, serious deformity may result from imperfect restoration of muscles after an attack of beriberi. Non-congenital talipes equinus is not uncommon in beriberi countries, and is probably in many instances consequent on this disease. Dilatation and hypertrophy of the heart, permanent cardiac bruits, muscular feebleness of legs and arms, circumscribed anæsthetic patches of skin and liability to œdema of the feet and ankles, have also been enumerated among the sequels of beriberi.

Diagnosis. — Under ordinary circumstances the diagnosis of developed beriberi, provided the disease be suspected, is not a matter of very great difficulty. Epidemic peripheral neuritis probably means beriberi.

In the early stage of the hydropic form it sometimes happens that distinct symptoms of peripheral neuritis do not declare themselves; for a time there may be no marked anæsthesia of skin, or hyperæsthesia of muscles, and the knee-jerks may be present or even exaggerated; œdema may be the only symptom. But in the presence of an epidemic of beriberi the rapid development of œdema, without albumin in the urine or other manifest cause, points to this disease. Any doubt which may exist is usually dispelled in a very few days by the appearance of the usual signs of peripheral neuritis.

From all similar forms of disease of the nervous system beriberi is distinguished by its epidemic character. As a matter of fact, the only real difficulty that is likely to arise in the diagnosis of beriberi from other nervous diseases is in the case of peripheral neuritis occurring in Europeans coming from a beriberi and malaria district. The question may then arise, is a given case beriberic, or is it malarial; or, if the patient's habits justify the suspicion, is it a case of alcoholic neuritis? Malarial neuritis of a character simulating beriberi is exceedingly rare: malarial neuritis limited to one nerve is common enough, and temporary cerebral disturbance from blocking of cerebral capillaries by the malaria organism is also not uncommon; but paresis of limbs, with muscular atrophy and implication of the heart and circulation, such as we find in beriberi, I cannot say I have ever recognised as a consequence of malaria. It is said, however, that such cases do occur, and that the symptoms exhibit a diurnal periodicity. I have seen well-marked splenic and hepatic enlargement in beriberi as a part of the disease, and apparently in no way symptomatic of malarial infection; such an occurrence, however, in a case of peripheral neuritis ought to put the medical attendant on his guard, and suggest examination of the blood for the malaria organism and pigmented leucocytes. If these are discovered, possibly the administration of quinine, by curing or relieving the paresis, might clear up the diagnosis. Even then one could not be sure that there had not been a combination of malaria and beriberi. In alcoholic neuritis œdema is not nearly so common nor so extensive as in beriberi. These considerations, together with the tremor, the gastric catarrh, the mental condition, and above all the history of drinking, should help to a correct diagnosis. It is very probable that in beriberi districts cases of double or even treble nerve poisoning from beriberi, malaria, and alcohol occasionally occur.

A paralytic affection called lathyrism, resulting from the use of a dal prepared from a lentil—*Lathyrus sativus*—prevails extensively in Upper and Central India, especially near Allahabad and in Upper Scinde. The same disease is found in Algeria. It is readily distinguishable from beriberi, being a spastic paralysis, evidently of spinal origin, affecting the lower limbs only, and associated from the outset with bladder symptoms as well as with exaggerated knee-jerks. There is no dropsy, no heart trouble, no anæsthesia, and no disturbance of the electrical reaction of the muscles [*vide* article on "Lathyrism" in this *System*].

The œdema, muscular pains and tenderness of trichinosis might suggest beriberi, more particularly as both diseases tend to occur in limited epidemics. But the seat of the pains in trichinosis—principally in the muscles of the trunk, head and neck; the violent gastro-intestinal disturbance preceding the muscle pains; the well-marked fever; the early œdema under the eyes and in the face; the absence of true paresis; the implication of the muscles of the eyes, face, and neck; the absence of pretibial œdema, of anæsthesia, of heart trouble; and the circumstances under which the malady occurs, should make diagnosis easy enough.

Besides the evidence afforded by the microscopical examination of the stools, ankylostomiasis may be distinguished from beriberi by the intense anæmia, the gastric symptoms, and the complete absence of symptoms of neuritis.

Malingering and hysterical mimesis are readily detected by an examination of the knee-jerks, by the electrical reaction of the muscles, and by the absence of œdema, cardiac irregularities and bruits.

Treatment.—In beriberi districts low-lying, damp localities should be avoided as building-sites or camping-grounds. If houses are built in such localities, the floor of the basement ought to be raised several feet and covered with a substantial layer of cement to obviate the damp, and the lower courses of the walls should be laid in stone. The sleeping-apartments ought to be well off the ground, efficiently ventilated, and never overcrowded.

In ships with native crews the officers must see to the proper ventilation of the forecastle, insisting on its being kept dry and clean, and preventing its being overheated by fires, lamps and overcrowding. The clothing of the men demands attention, and their wet garments ought never to be hung up to dry in the sleeping-quarters. The men, too, ought to be kept on deck as much as possible and out of their stuffy quarters.

The dietary should be liberal and varied, with not too large a proportion of rice—wheat, barley, oats, or beans being substituted for that cereal.

On the occurrence of a case of beriberi in a jail, camp, school, plantation, mine or ship, prompt measures must be taken to prevent the spread of the disease. The entire community should be examined for symptoms of latent peripheral neuritis, their knee-jerks tested, œdema looked for, and their leg muscles examined for evidences of hyperæsthesia. Schools should at once be broken up; in jails the prisoners should, if possible, be removed from the quarter in which the disease appeared; camps should be shifted; on plantations and mines such measures should be adopted as our knowledge of the habits and nature of beriberi and the circumstances of the case suggest; on board ship the crews' quarters must be cleansed, disinfected, white-washed, and ventilated, and, if practicable, the men sent to sleep elsewhere. In all cases the dietary must be inquired into and supplemented if found insufficient.

The first and most important thing to be attended to in the treatment of a case of beriberi is the removal of the patient from the room, and, if possible, from the house and neighbourhood in which the disease was acquired. In Japan and in Java it has been found that sending beriberi patients to some high and dry spot is generally followed by rapid improvement. In Singapore a similar result followed sending beriberi-smitten prisoners to sea for a short time. In the cases of beriberi brought to the Seamen's Hospital, Greenwich, from ships in the London Docks, it is found that if they survive the first few days on shore they steadily recover. It may be laid down as an axiom, that in all cases of beriberi the chances of recovery are very much prejudiced if the patient remain in the tainted spot.

The diet ought to be fairly liberal, bulky articles of food being avoided. Rice, therefore, being of a bulky, distending character, should be given only in very small quantities, its place being taken by wheat, barley, and beans. The Japanese use in beriberi a bean they call "adjuki" (*Phaseolus radiatus*), which they cook and eat alone or mixed with barley and rice. This bean is markedly diuretic.

If the case be a mild one, the patient, suitably clothed, should be encouraged to keep out-of-doors; but if it be a severe one, especially if there be signs of cardiac weakness, he ought to be kept at rest in bed.

Quinine, salicylate of sodium, arsenic, nitrate of silver, belladonna, caffeine, treeak ferook, are some of the many drugs which have been advocated from time to time; but, so far as known, there is no medicine which has a specific influence on this disease. The drug treatment resolves itself, therefore, into a treatment of symptoms.

My routine practice has been to counteract constipation at the outset, and to relieve the accumulation of fluid in the tissues by the administration of small and frequently repeated doses of sulphate of magnesium or sodium; combining the aperient, where there is evidence of cardiac debility, with small doses of digitalis. When the disease is subsiding, the aperient is omitted and iron substituted. Later, when muscular hyperæsthesia is diminishing, strychnine with massage and faradisation are prescribed.

Cramps and excessive muscular hyperæsthesia may be treated by anodyne liniments, bromide of potassium, or tincture of aconite.

When symptoms of cardiac failure appear from over-distension of the right heart—and it must be borne in mind that they often do so appear, and quite suddenly even in what seems to be a very mild case—treatment must be prompt and energetic; otherwise death is nearly sure to ensue. Therefore on the appearance of marked breathlessness, palpitations, substernal pains and distress, cyanosis, and such symptoms, a full dose of nitro-glycerine or of nitrite of amyl should be administered at once. Simon, who has had large experience, recommends five to ten minims of the one per cent solution of the former, to be repeated every quarter or half-hour as symptoms indicate. At the same time a quickly-acting and energetic cathartic, such as croton oil, or elaterium with or without calomel, should be administered. If these measures do not speedily give relief the only chance of saving the patient is to bleed him from the arm or neck. This often staves off immediate danger, and gives time for other measures to act. As the phlebotomy may have to be repeated, it is not advisable to take more than five or six ounces of blood at a time—just sufficient, that is, to relieve the labouring heart. In desperate cases aspiration of the right ventricle has been recommended.

Hydrothorax and hydropericardium must not be overlooked; if effusion be considerable, aspiration may be necessary.

PATRICK MANSON.

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P. M.

MALTA FEVER[1]

SYNONYMS.—The following are a few of the many names which have been given to this disease at different times: *Gastric remittent* and *Bilious remittent fever*; *Mediterranean fever*; *Mediterranean gastric remittent fever*; *La febbre gastro-biliosa*; *Fæco-malarial fever*; *Intermittent typhoid*; *Adeno-typhoid*; *Febris complicata*; *Febris sudoralis*; *Typho-malarial fever*; *Pythogenic septicæmia*; *Rock fever*; *Neapolitan fever*; *Danubian fever*, etc.

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[1] Some nosologists object to the name "Malta" fever. The name seems to me to be sufficiently unobjectionable—as unobjectionable, for instance, as the names "muslin," "calico," and "damask." The list of synonyms, at any rate, makes one despair of a better.—ED.

Short Description.—An endemic fever of long duration (usually lasting from a few weeks to many months), accompanied by profuse perspiration and constipation, and often followed by pains of a rheumatic or neuralgic character, with swelling of the joints or orchitis, and tenderness and enlargement of the spleen. The disease is further characterised by a small mortality, tedious convalescence, a constant liability to relapses, and well-marked anæmia. It is not contagious.

History.—On this point one is unable to obtain much light by historical references. In the *Epidemics* of Hippocrates there are passages which, making allowance for the differences between the modes of thought and expression of his day and those of our time, might almost pass for a brief description of the disease.

The earliest mention of this fever is found in the reports of the medical officers of the army and navy in the early part of the present century. That it undoubtedly existed not only in Malta, but also in other parts of the Mediterranean, is very clear from those reports. Burnett, writing on the fevers of the Mediterranean in 1816, describes this disease as being one of a severe remittent malarial character. It was equally prevalent among the British occupants and the native population, but in both possibly somewhat modified by the food and insanitary conditions existing at that date. That it was the same fever as we are now discussing is evident from the statements, "Though fevers are more common than in England, they occasion less mortality than in the United Kingdom"; and again, "Rheumatism was common, and often extremely intractable."

In the few published writings of the older medical officers of the army and navy it does not appear that the primary fever of this disease was distinguished from the malarial remittent or continued fevers. It was not till after the Crimean war that the distinction began to be made. During the last twenty years, however, not only has this been done with increasing frequency, but the connection between the primary fever and its sequels has been more and more clearly seen.

Geographical Distribution.—The island of Malta, from which this fever takes its name, is situated about 60 miles from Sicily, and nearly 200 miles from the African coast. It is of irregular oval shape, about 12 miles from north to south, and 20 miles from east to west. The surface presents the appearance of an inclined plane, sloping gradually to the south-west. The whole substratum is composed of a soft calcareous sandstone, and is but scantily covered by soil.

The island contains neither river nor lake, and from its geological structure and the absorbent nature of the soil has little marshy or swampy ground. There is no exuberant vegetation, brushwood or forest; the verdure is scanty, and the greater part of the surface presents nothing to the view but the arid rock.

The most prevalent winds are from the south-east, south and north-west. That from the south-east, termed the sirocco, is common, and prevails principally during the autumnal months.

The annual mean temperature is 68° F.; the hottest month (July or August) is 81° F.; the coldest month (January), 55° F.; the extreme yearly range (from highest to lowest temperature in the shade) is 56° F., namely, from 96° F. in July to 40° F. in January; the mean yearly range is about 48° F.

The rainfall is about twenty-four inches, the greater part of which falls in November, December and January. During the summer months the island is almost rainless.

That the fever is not confined to Malta there is now ample proof. It has long been recognised as identical with the "rock fever" of Gibraltar, which view Donaldson (8) also confirms. Veale (8), who has seen many cases, believes that the fevers of Malta, Gibraltar and Cyprus are all one and the same disease. In Italy it has been described as occurring at Naples, Benevento and Civita Nova del Samo. Tomaselli has seen a large number of cases in Catania in Sicily. In Constantinople, according to Patterson, this fever is common, and is known under the vague term "country fever." Capetanakis states that this fever tends to become frequent in the town of Candia, and is known by various names, such as "Italian fever," "Neapolitan fever," and so on. Apparently it was unknown there a few years ago (Bruce). Milnes (6) states, as the result of three years' careful study of this disease, that he is convinced it is prevalent in all parts of the shores of the Mediterranean and Red Sea; a case of fever at Sawàken or Massowah will not present features very different from those of a case at Malta or Naples.

Oliver (7) has seen and treated cases of fever contracted on the banks of the Danube which were neither pure malaria nor enteric fever. The cases were characterised by long duration, small mortality, and frequent relapses.

From this brief summary it is clear that this fever is not limited to any one place, but appears to diffuse itself over a wide area within the subtropical regions. In its secondary stage, in persons who have contracted the disease in its endemic home, it may be seen in this country; but it has never originated or spread in this climate.

Like other diseases belonging to the tropical and subtropical zone, it is most frequently found near the shores of the sea-coast and on the banks of large rivers; inland places being comparatively free from its attacks. It prevails chiefly during the hot months of the year.

Period of Incubation.—The conditions under which Malta fever occurs often render it very difficult to arrive at a definite conclusion as to its period of incubation.

Undoubtedly we have some few facts showing with tolerable accuracy the time that has intervened between the exposure to the cause and the invasion of the illness. Chartres states that six days after the 100th Regiment occupied Verdala Barrack at Malta cases of this fever began to be admitted to hospital. Marston says that ten days is the probable incubation period, and gives two cases to justify his conclusion. These are instances no doubt in which the fever has been somewhat sudden in its onset; but there are many cases in which the attack comes on slowly and insidiously, and in which it is impossible to fix any limit.

On account of the long duration and the constant relapses which take place during the progress and course of this disease, it is impossible to state whether one attack confers an immunity from a second. The question is still undecided. Bruce is of opinion that such is the case.

General Symptoms.—The invasion of the disease may be sudden or gradual. The symptoms in the early stage are rather obscure. The attack is preceded generally by dyspepsia, languor, headache, chilliness, and great weakness; it is often accompanied with muscular pains. The preliminary stage is usually marked by loss of appetite, often by headache and backache, but seldom by rigor or vomiting. Symptoms of gastric derangement manifest themselves at an early period, and persist more or less to the end. After a few days the patient suffers from nausea, sometimes even vomiting; his bowels are generally constipated, though there may be diarrhœa. He feels chilly and feverish, and recognises that his illness is increasing day by day.

In the more severe forms intense frontal headache is present, with enlargement and tenderness of the spleen. The patient's lassitude and debility become so great that he ceases to take an interest in anything; he loses his appetite altogether, and throughout the whole day and night he remains hot, thirsty, ill and desponding. There is sometimes an extraordinary feeling of restlessness, and this is frequently associated with insomnia. These symptoms may decline after a variable period, rarely less than a week, more frequently extending to two or three, when the patient fancies himself convalescent. But in a day or two relapses occur; his nausea or vomiting returns, with loss of appetite and constipation, which may be followed by diarrhœa of a dysenteric character; the stools are devoid of any offensive odour; they may contain mucus and blood, but they are usually dark-coloured, and are never like those seen in enteric fever. Muscular pains increase; the patient now becomes very anæmic, and his spleen is enlarged and painful on pressure.

In the more severe cases many or all of the preceding symptoms are aggravated; the headache becomes so intense as to be scarcely endurable, and the drowsiness may merge into stupor with low muttering delirium; the prostration is extreme; the lungs become congested, and readily take on a low form of inflammation; there may be epistaxis or sometimes considerable hæmoptysis. The pain in the limbs may develop into very decided rheumatism, with effusion into the joints. Endocarditis or other complications may supervene, and death ensue at almost any period.

Digestive System.—The symptoms of gastric and intestinal catarrh manifest themselves at an early stage, and persist more or less to the end. The tongue is coated white with red edges, and the papillæ are prominent at the base; it is large, flat and flabby, and sometimes marked with the impress of the teeth. As the disease advances the tongue becomes more or less coated in the middle, and red at the tip and edges. Veale has found this condition so constant that, so long as it remains, he never considers a man free from the tendency to relapses.

The tonsils are often enlarged and swollen; the pharynx congested, and occasionally ulcerated. The gums may be spongy, and may bleed freely; sometimes they are raw, sore, and slightly ulcerated. The palate is at times coated with an aphthous deposit, but there does not appear to be any inclination for this to spread. There is generally some uneasiness at the stomach, with a feeling of nausea after food; but vomiting in the early stage of the fever is uncommon, and betokens either a severe attack or the early stage of a relapse. The appetite varies; when there is no nausea it is usually good.

The bowels are, as a rule, constipated, particularly in the milder cases, but there are many exceptions to this; they are seldom regular, often confined, and as often as not the patient suffers from diarrhœa, the evacuations being as described above. The abdomen may be tympanitic, but this is unusual. The spleen is always enlarged, and pressure over it causes pain, even in those cases which are otherwise convalescent. The liver is sometimes enlarged, and may be tender on pressure, but in my own experience the enlargement of this organ is not constant or easily demonstrated. When pain is complained of it is invariably the left hypochondriac region that is referred to, and not the right.

Respiratory System.—There is a very general tendency in this disease to bronchial and catarrhal affections. About the end of the second or the commencement of the third week evidences of congestion of the lungs appear, the apices being the parts chiefly involved. The severity of the cough and expectoration are generally out of all proportion to the physical signs. On auscultation sibilant, mucous and rhonchal râles are heard; on percussion there is somewhat diminished resonance. This, in severe cases, may be followed by congestion of the lower and posterior parts of the lungs, rapidly passing into pneumonia, accompanied by pleurisy and effusion; in almost every case it occurs on the left side. The dyspnœa and the amount of blood in the sputa are out of all proportion to the conditions found on physical examination. In the more severe forms of the disease this inflammation assumes a chronic character, and chronic pneumonic phthisis may follow.

Circulatory System.—Palpitation is by far the most common symptom. With the least excitement the heart beats with unusual rapidity, and "hæmic murmurs" become audible. The pulse ranges from eighty to ninety beats per minute, and seldom exceeds this during the first period of the disease: during the later stages the pulse gains in frequency and loses impulse. Purpura frequently complicates this disease, and epistaxis, hæmoptysis and bleeding from the gums are common. The red blood corpuscles as a rule fall from 5,000,000 per cubic millimetre to about 3,500,000. The white blood corpuscles in most cases are found to be normal in number (Bruce).

Temperature.—The temperature curve in Malta fever is extremely irregular; so much so, that it is impossible to present any one case or single chart as characteristic of the disease.

In the early stages the range of temperature usually presents a continued form of fever, with slight exacerbations of temperature in the evening not exceeding one or two degrees, the temperature ranging between 102° and 104°. In mild, uncomplicated cases this condition lasts for a week or ten days, when the normal temperature is reached, and convalescence is established.

In less favourable cases, when relapses occur after an interval of ten or twelve days, a second increase of temperature takes place, lasting about ten to twelve days; when again the normal line is reached. This may be followed by another relapse with a somewhat longer interval, and with a shorter period of fever; after this the temperature again becomes normal, and with comparatively few exceptions this disturbance ends.

Frequently in the secondary stages of the fever the temperature, during pyrexial periods, presents the remittent form. In the early morning and forenoon the temperature in the axilla and under the tongue is most frequently between 97° and 101°; but in the afternoon it rises more or less, generally from two to four degrees, and continues high until midnight, or perhaps a little later, when defervescence sets in with perspiration (Veale).

In fatal cases the temperature usually runs up rapidly, shortly before death reaching 110°.

Nervous System.—The face and expression are truly characteristic of this fever; the pallor, anæmia, weariness and despondent manner betoken the virulent nature of the poison and its effect on the nervous system. Delirium, as a rule, is confined to the more severe cases. Insomnia is frequently mingled with an excessive irritability which is often associated with loss of memory.

In the secondary stage these symptoms become more conspicuous. The patient is weak, tremulous, almost timid, and ready to shed tears on the least provocation. More rarely one may observe aphonia, or a temporary loss of sensation or of motion in the extremities. These deviations from the normal state exist in various degrees: sometimes one, sometimes another assumes a special pre-eminence. The shock to the nervous system, after the graver attacks, remains for some time. The memory is considerably impaired, especially with regard to names and dates, or rather the chronological order of events; the power of concentrating ideas, or following out a train of thought, is temporarily destroyed, and but very slowly returns. We must not mistake the mental aberrations, the aphonia, anæsthesia, hyperæsthesia, and so forth, for symptoms indicative of permanent lesions of the brain or spinal cord (Veale). Neuritis, especially in the form of sciatica, is apt to occur.

Genito-urinary System.—One of the most painful complications of this fever is inflammation or neuralgia of the testicle; it occurs in about 15 per cent of the cases. The epididymis is the part most usually affected, but not infrequently the body of the testicle is involved also. The inflammation usually subsides without any active treatment. The average daily quantity of urine passed is between fifteen and twenty-five ounces; it is neutral, or very slightly acid when passed: there is usually a deposit of lithates and phosphates, but, apart from pre-existing kidney disease, albumin is extremely rare. In very severe attacks bile may be present in the urine.

Integumentary System.—Pallor and anæmia are perhaps the most characteristic features in the early stage. A condition approaching jaundice may also be present, but this is unusual. Perspiration is profuse, and sudamina, in greater or less number, are almost an invariable accompaniment. Cutaneous eruptions, such as erythema, eczema and erythema nodosum, are not uncommon in the secondary stage. Many patients complain of a tingling or pricking sensation in the face, forehead or hands, without any condition to account for it, except perhaps the nervous state already referred to. The hair falls out in nearly every case, usually during the secondary stage when the rheumatoid pains and swellings are most severe.

Articulations.—The rheumatic pains rarely if ever occur during the early stages of the disease. There is no constancy in the order in which the joints are affected. Sometimes the small joints of the hand or foot suffer first. In my own experience the extremities were most frequently involved, and the ankle-joint by preference. The joints became exquisitely tender, not in consequence of the amount of effusion present which is often inconsiderable, but from the hyperæsthesia of the integument.

The most painful of all the joints are the sacro-iliac, in which the least movement causes the most intense pain. In such cases every change of position is dreaded, and the patient lies for days in the same position, risking the formation of bed-sores, and resisting the desire to evacuate the bowels, in order to avoid the suffering that the movement entails.

The tendo Achillis and the fibrous structures round the ankle-joint are frequently implicated and exceedingly painful; oftentimes the lumbar aponeurosis and the sheaths of the nerves issuing from the sacral plexus are affected, and the pain runs down the back of the thigh or radiates to its anterior surface.

Occasionally, as in gout, the bursa over the patella fills with fluid and becomes painful; but, more frequently, painful, node-like swellings form on the ribs or on their cartilages, or even on the sternum itself; these have been observed in patients who had not presented a sign of syphilis, either congenital or acquired.

Etiology.—Until the appearance in 1887 of Bruce's classical and scientific accounts of the fever, nothing definite was known as to its causation. From the accessible data available from statistics and records of the Army Medical Department (8) during the present century, and from the prevalence of its attacks during certain periods of the year, it was early apparent that its presence in Malta and Gibraltar was connected with fæcal and organic matter from human sources.

The earlier writers are of opinion that the poison may be diffused in the air, and that it enters the human system by way of the respiratory passages. Tomaselli therefore alleged that it is a fever of miasmatic origin; otherwise, he says, he was unable to account for its rapid diffusion on a large scale.

In Naples this fever is said to frequent the low-lying parts of the town, and those localities especially where the sewers are discharged.

Sewers and sewage works, where these have been undertaken, as in Valetta and Naples, appear to have had little influence in diminishing the attacks. Indeed these channels are so frequently pervious, and allow the fæcal matter to soak into the pores of the soil, that they virtually become elongated cesspools, and increase rather than diminish the dissemination of the poison.

Tomaselli notices the same fact in relation to the prevalence of the fever and the introduction of sewers into Catania. In his opinion, the immense quantity of sewage and sewer-air, which is developed in these sewers and finds its way out of them, is to be placed in the front rank of its causation; and is an argument in favour of the aerial dissemination of the morbific agent. This condition is intensified when, during periods of drought, the sewers from want of flushing contain putrefying deposits which exhale poisonous miasms. The same fact has also been observed in Malta, where an imperfect system of flushing the sewers, when these were first laid down, was followed by an increase rather than a diminution of attacks.

On the other hand, although there is no positive evidence to prove that food and water are vehicles for the dissemination of this poison, we are compelled by analogy to admit the extreme probability that Malta fever, like enteric, is chiefly diffused by means of drinking-water or other fluid, or solid foods, to which the poison has gained access. In this belief Bruce, who had a considerable practical knowledge of the disease, concurs; and certainly the facts above mentioned are not inconsistent with this alternate view.

As regards its remoter causes Malta fever differs somewhat from enteric fever. In the latter disease all observers agree that the predisposition is greater in childhood and early adult life; especially between the ages of twenty and twenty-five. On the other hand, although Malta fever is found in the young and in adults, men up to thirty-five years of age seem to suffer in the same proportion as those whose ages are between twenty and twenty-five. Tomaselli is of opinion that the greatest number of cases occur between six years and thirty years of age; a smaller number between the ages of two and six, and thirty to fifty; and very few above fifty. Sex appears to have little influence, but the disease is perhaps more common among men than women.

It would seem likely that intemperance, by diminishing the powers of resistance in the individual, would increase the liability to contract Malta fever, but there is no proof that it does so. Few patients admitted to the military hospitals can be classed as intemperate, and none are broken down by this cause. There is no evidence that grief, fear, or other emotion enters into the causation, and the same may be said of bodily fatigue and overcrowding.

That Malta fever occurs in an epidemic form there can be no question. Marston (8) states that it alternates with enteric fever; and that when the latter disease is prevalent Malta fever is in abeyance. Bruce has noticed the same alternation, and Tomaselli regards the fevers which occurred in Catania in 1872 and 1878 as different epidemics.

We find other characters which mark this fever as distinct from enteric. In enteric fever it is well recognised that the largest number of cases do not occur at the period of greatest heat, but usually from six weeks to two months afterwards; and the minimum is not reached until about the same length of time after that of the most intense cold. On the other hand, the season of the greatest prevalence of Malta fever is July and August, and the fewest number of attacks are in December—the two former being the hottest months, and the latter having a mean temperature considerably above the minimum.

This fever is not contagious. In the hospitals at Malta patients are treated in the general wards and have never been known to infect others. Tomaselli also states that he is of this opinion, and relates that members of a family were known to occupy, not only the same room, but also the same bed with a sufferer, and yet remain in the best of health; and further, he observed isolated cases in the country which showed no tendency to spread.

It may also be remarked that the disease attacks those occupying large and well-ventilated houses as well as soldiers in barrack-rooms, and probably in an equal proportion.

Morbid Anatomy.—Of the morbid anatomy of Malta fever there is not very much to be said. The principal appearances found on post-mortem examination are those due to fever, accompanied by a high temperature, and the presence of some irritating poison in the blood. The serous, muscular, mucous and submucous layers of Peyer's patches, if examined under a low power, are found normal; and the epithelial layer is continuous over the whole surface of the gland. Under a higher power any morbid changes are found restricted to the mucous and submucous layers, and consist in a slight proliferation of the cellular elements. The small intestine is usually pallid and anæmic, except in the duodenum and upper part of the jejunum, where the mucous membrane may be more or less congested; in the more severe and chronic cases this may be accompanied by atrophy of the lower portion of the ileum. The large intestine is frequently extremely congested, especially the cæcum. The mesenteric glands are but slightly enlarged. The spleen is usually very much enlarged, dark on section, and the pulp soft and friable: it may weigh as much as sixty ounces; the average weight is eighteen ounces (Bruce). An appearance of intense congestion is seen on section, the sinuses being enormously distended with blood.

The liver is congested, and presents a pigmented appearance on section; and there is small round cell infiltration between the lobules.

The kidneys are usually congested, with slight signs of hæmorrhage into their substance. The capsules are easily separated.

Bacteriology.—Like enteric fever and other infectious diseases, Malta fever is due to the introduction into the system of a micro-organism first described by Bruce (1) in 1887; and to it he has given the name of "micrococcus Melitensis." As it is apparently absent from the blood, it has hitherto been almost impossible to demonstrate its presence during life. The organ in which these micro-organisms occur in the greatest numbers is the spleen; and it is only by withdrawing a small quantity of splenic blood by means of a sterilised hypodermic needle that its presence during life has been demonstrated (Bruce).

The micro-organism grows best in nutrient material, the alkalinity of which is slightly less than human blood, and at a temperature of from 37° C. to 39° C. It fulfils Koch's postulates at all points.

On a sloping surface of 1½ per cent of peptone agar, at a temperature of 37° C., its colonies become visible to the naked eye in from 120 to 125 hours after inoculation from the human spleen. They first appear as minute, transparent, colourless drops on the surface of the agar. In about thirty-six hours they assume a transparent amber colour, and, increasing very slowly in size, become opaque in from four to five days from their first appearance. No liquefaction takes place. The colonies retain their vitality for over three months, although they do not increase after two months. They cease to grow at 18·5° C., and die if kept long at a moist temperature below 15·5° C.; they live, however, for a long time in the dry state. They will not grow as primary growths on agar having an alkalinity in excess of the blood. They can also be cultivated on gelatine and in bouillon: in the former very slowly at a temperature of 22° C. without liquefying; in the latter they give rise to a general and increasing opaqueness, commencing on the fifth or sixth day, and afterwards forming a white precipitate consisting of these cocci, without forming a surface pellicle. Microscopically, in the hanging drop they appear as very minute cocci $0·33\,\mu$ in diameter, ovoid or nearly round in shape, in rapid molecular motion, and at times to be seen in chains of two or more.

They stain readily with gentian or methyl-violet and fuchsine, but lose their stain rapidly if treated with alcohol. Mounted in balsam they appear as minute cocci here and there arranged in short chains. They can be observed in fresh splenic substance, and, during life, in the splenic blood of men suffering from this fever. The blood and spleen show no trace of the malaria parasites (Thin).

Mortality.—The immediate mortality from this disease is small. Bruce (1) states that it is not above two per cent, and my own experience confirms this. Danger, however, is to be apprehended from continuously high temperature, and from such complications as pneumonia and endocarditis. Excessive anæmia may also lead to fatal syncope.

Treatment.—The only principle on which we can treat this fever is the rational one of supporting strength and combating symptoms as they arise. It has hitherto been found impossible by any remedial means to arrest the disease. In the early stage, if the patient suffer from constipation, some mild laxative may be given. Except at the very beginning of the fever, a hot bath is scarcely to be recommended, as the depression produced by the disease is already sufficiently well marked.

To relieve the nausea and vomiting a draught of morphia and hydrocyanic acid repeated occasionally, or again a few minims of chlorodyne, generally prove useful.

For the diarrhœa, when the ordinary vegetable astringents have failed, and especially where the hæmorrhagic tendency has been a source of danger, the continued use of the tinctura ferri perchloridi seemed to be most beneficial. Ergot and ergotine have also been of service in arresting hæmorrhage when profuse.

Opiate enemas are especially useful in checking the milder forms of diarrhœa, and are as a rule extremely grateful to the patient.

Quinine has been given in doses varying from three to eighty grains daily, but without any beneficial effect. It neither arrests the progress of the fever nor limits the night sweats or the rheumatic pains.

The hypodermic injection of morphia and the liniments of aconite, opium, and belladonna are useful in relieving the lumbar, sciatic and articular pains; salicylic acid and the salicylates are quite useless; and the same may be said of blisters, which appear only to substitute temporarily one pain for another. Orchitis is best relieved by hot fomentations, to which belladonna or opium may be added, and by the support of the inflamed testicle.

In cases in which the temperature curve rises suddenly the application of cold is probably the best antipyretic. Cold sponging and the wet pack are useful in moderate cases; but when hyperpyrexia threatens, immersion of the body in a cold bath is necessary to save life. The bath should be at a temperature of 68° F., and its duration should be about ten minutes; if, however, the patient show signs of great weakness it should not exceed five minutes. After the bath the patient should be wrapped up in a dry sheet or a light blanket and put to bed: the temperature should be frequently taken, and the baths repeated as often as the temperature rises to 103° F. or above it. Should the pulse show signs of failing, or if there should be shivering or any other evidence of weakness, brandy or some diffusible stimulant should be given, and bottles containing hot water applied to the feet. The cold bath should not be used except in cases of hyperpyrexia of such intensity that death seems imminent and only to be averted by energetic treatment.

Antipyrin is useful when given in full doses at intervals of an hour, or two or three hours. It causes a fall of temperature in a short time, which however rises again as rapidly. Headache and muscular pains are largely benefited by the use of this drug, and in the early stages it removes sleeplessness.

Careful nursing is perhaps the most important agent at our disposal. Food should be frequently administered, and the patient enjoined to make an effort to retain it. In many cases food of a semi-solid nature will be tolerated when liquid food is rejected. The diet should be very light, food of the simplest and blandest description, such as milk, beef tea, and chicken jelly flavoured with a little lemon, being appropriate.

Stimulants in the early stages of this disease are not to be recommended. When required they are best taken in the form of iced Moselle and soda water given as an ordinary drink, which not only slakes the burning thirst of the fever, but also allays to a considerable degree the irritability of the stomach. When the object is simply to slake thirst, lemonade made from the fresh juice of the fruit ought to be given, as this prevents the occurrence of scorbutic symptoms.

After the acute stage of the fever has passed the diet may be varied as much as possible, rice and custard puddings, fish and white meat being taken; but the return to solid food must be gradual. Until the temperature has remained normal for at least a fortnight the patient should not return to his ordinary diet.

Convalescence can rarely be completed without a change of climate; most patients rapidly regain health when transferred to this country. It is, however, essential that this transportation should not take place during the first stages of the disease, but when convalescence is partially established.

J. Lane Notter.

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J. L. N.

EPIDEMIC DROPSY

In the year 1877 an outbreak of a disease, whose principal feature was dropsy, occurred in the southern suburbs of Calcutta. It continued to prevail during the cold season of 1877-78, disappeared in the hot weather, recurred over a wider area in the cold months of 1878-79, subsided again in the hot weather, broke out a third time over a more extensive area of the town and suburbs in the cold season of 1879-80, and finally vanished in the hot weather of 1880. The new ground invaded in each recrudescence was contiguous to that which had been previously occupied, but isolated offshoots also occurred: the larger and more distant of these were a well-defined outbreak in the hill station of Shillong, in the Khasia Hills, Assam, in the winter of 1878-79; and a somewhat severe prevalence among natives inhabiting the city of Dacca in Eastern Bengal, and among coolies employed in the tea gardens of South Sylhet during the same time. A similar epidemic broke out in the island of Mauritius in November 1878, and continued to prevail extensively until April 1879, when it died out. Labourers for the tea gardens of Assam and Sylhet, and for the sugar plantations of Mauritius, pass through Calcutta; the latter embark at the place where the disease first made its appearance.

This remarkable epidemic of dropsy was very carefully observed in each locality, and its phenomena—clinical and epidemiological—have been minutely recorded by Davidson, O'Brien, Crombie, and others. At first it was thought to be a manifestation of beriberi, in many cases of which dropsical effusions into the cellular tissue and serous cavities take place. On closer study of the disease, however, it became clear that, although dropsy occurs in both affections, these presented striking differences in every other respect. Recent researches have demonstrated that beriberi is essentially a peripheral neuritis; in the Calcutta and Mauritius disease neurotic symptoms held a very subordinate position, and the anæsthesias and palsies observable in every case of well-developed beriberi were absent. Epidemics of dropsy have been repeatedly observed both on land and at sea; but it is difficult, owing to the vague description and imperfect identification of these, to decide whether they were instances of "wet" berberi, or of a disease similar to that observed in India and Mauritius, the facts of which are summarised in the following description:—

Symptoms.—Pyrexia, gastro-intestinal disturbances, burning and pricking of skin, and deep-seated pains in body and limbs were the most common initial symptoms. In a considerable proportion of cases, however, anasarca was the first indication of disturbed health, and the symptoms just mentioned accompanied or succeeded the dropsical swelling. The dropsy was an invariable and essential feature of the complaint, and was always either initial or early. The lower limbs were affected in the first instance, the trunk and upper extremities subsequently in severe cases, the face rarely. The effusion was in most cases confined to the skin and subcutaneous areolar tissue; œdema of the deeper cellular tissues took place in severe cases; the serous cavities of the chest—pleuras and pericardium—were sometimes filled with serum, the peritoneum and arachnoid cavity very seldom. The anasarca of the lower limbs often persisted after every other morbid condition had disappeared. The pyrexia was of mild type; seldom preceded by rigors or resolved by sweats; remittent, with morning temperatures of 99° or 100° F., and evening temperatures of 100° or 101° F. In some few cases, when the lungs became congested or inflamed, higher readings were noted. Vomiting and diarrhœa were frequent premonitory events, and diarrhœa and dysentery sometimes appeared during the course of the attack, and were apt to be troublesome and exhausting. Itching, burning, and other unpleasant sensations often preceded and accompanied the development of the anasarca, and in a considerable proportion of cases the surface became erythematous or affected with an urticarial, scarlatinal or morbillous rash. Phlyctenæ and petechial and purpuric spots were also observed. These rashes appeared in the earlier stages of the attack; eczema, desquamation, excoriation and ulcers were occasionally observed later. The deep-seated pains probably depended on the pyrexia, and occurred within the first fortnight. The condition of the urine varied as regards colour, quantity, specific gravity, and frequency of discharge. No tube-casts or albumin were found. In severe cases respiration and circulation were much disturbed. The cough, dyspnœa, and orthopnœa observed in some cases were evidently due to œdema or congestion of the lungs, and effusion into the cavities of the chest—conditions which occasionally caused sudden death. Anæmia was a prominent and constant feature of the disease, which in Mauritius received the name of "acute anæmic dropsy." The red corpuscles were diminished in number, the leucocytes increased, and an unusual amount of granular and molecular material was observed in the blood. The disease in severe cases produced considerable prostration and emaciation. No enlargement of the spleen was noticed, but in some cases, in which cardiac and pulmonary complications existed, the liver was found to be tender and its area of dulness extended. Neither anæsthesia nor paralysis was observed, though these symptoms were carefully looked for both in India and Mauritius. The duration and severity of the disease varied considerably. From three weeks to three months may be stated as the limit of duration. Debility, anæmia, and persisting œdema of the legs were the only sequels observed. The case mortality varied between 2 and 8 per cent. Some Calcutta returns gave higher figures, but they probably included an excess of fatal cases. Death was caused mainly by pulmonary and cardiac complications, and in some cases was sudden and unexpected. Post-mortem examination revealed effusions and congestions. The subcutaneous effusion was in some cases hard and sanious. Punctate extravasations of skin and serous surfaces were observed; congestions of stomach and intestines, of the liver and mesenteric glands, and cloudy swelling of the renal epithelium, were also noted. No bacteriological investigations were made either in India or Mauritius.

Epidemiology.—The variety of geographical and meteorological conditions under which the disease prevailed indicated that place and season had no important influence in the causation of this malady. The curious Calcutta experience of three outbreaks, with two intervening periods of latency, showed that the conditions existing in the cold season were more favourable to its development and spread than those obtaining during the hot weather and rains. It was also in the cold season that the disease prevailed in Shillong, Dacca and South Sylhet; but in Mauritius neither temperature nor humidity, rain nor drought, elevation nor soil, seemed to affect the course of the epidemic. The element of malaria may also be eliminated. Nor did food or water, shelter or clothing, cleanliness, comfort or general salubrity appear to govern the origin and spread of the disease; though unfavourable personal and hygienic conditions probably affected the issue in individual cases, and aggravated the severity of seizures and the general mortality. In the years 1876 and 1877 Southern India was visited by a terrible famine, and scarcity and dearness of food prevailed in Bengal at the time when the disease appeared in Calcutta. Numbers of starving people flocked into that city from the famine tracts, and fever, cholera and small-pox were more than usually rife and deadly; but this dropsical disease was by no means confined to the impoverished and sickly; and in other localities which it visited such conditions were absent. Natives of India were the chief or only victims of the malady, which appeared and spread, in the first instance, among the members of a particular section of the native community, and then extended to other sections more or less associated with them. In Calcutta, Mohammedan tailors and boatmen were first attacked; and subsequently native villagers of all races and castes living in the same or adjoining hamlets. A few Eurasians and Armenians suffered, but no European. In Shillong, Bengalis were primarily and principally the sufferers; later a few hillmen and Goorkhas took the disease. In Dacca the disease prevailed among natives only, and in Sylhet among the garden coolies exclusively. In Mauritius it broke out among Indian labourers, and prevailed most among those imported from Calcutta. The general population subsequently suffered, though to a smaller extent. Adults were the most numerous victims, and males were attacked in larger proportion than females; but children were not exempt, and among these sex proportion was more equal. The outbreaks in all places presented the character of an epidemic rather than an endemic. Neither before nor after the outbreak did any disease presenting similar symptoms exist endemically or appear sporadically in any of the places visited.

There is some ground for belief that the disease was originally imported from the Madras famine tracts. Dr. Rammay Ray, who had been on famine duty, had treated 500 cases of a dropsical disease in the famine country, which was called beriberi; and on his return to Calcutta he identified the malady which he found there prevalent with that which he had seen in Madras. Calcutta was undoubtedly the centre from which the disease was carried to other places—to Dacca, Sylhet, Shillong and Mauritius. The spread of the disease was accomplished by human agency and intercourse. The manner in which it grew in households and communities proved its communicability, and numerous instances of grouping and importation were recorded. Its diffusibility was, however, by no means keen nor its incidence strong. In Mauritius, where the conditions of prevalence seemed to be more favourable, only about one-tenth of the persons exposed to the risk of contracting it suffered, and in other places the proportion of victims was less and margin of immunity greater.

Diagnosis.—The only disease with which epidemic dropsy is likely to be confounded is beriberi; but on comparing the clinical and epidemiological characters of the two diseases a radical distinction between them becomes apparent; there ought in future to be no difficulty in discriminating the one from the other. Beriberi is a peripheral neuritis of which dropsy is not an invariable accompaniment; epidemic dropsy partakes more of the nature of an exanthem; the dropsy is a constant feature, and the nervous phenomena characteristic of beriberi are absent. Epidemic dropsy is a febrile disease; in beriberi fever is either masked or absent. The congestions and eruptions observed in epidemic dropsy are rare or absent in beriberi. This is also true of the gastro-intestinal disorder so frequently seen in the former. Beriberi is a more severe, protracted and fatal disease; it is also an endemic rather than an epidemic, the opposite being true of epidemic dropsy: the former has also more definite geographical limits than the latter, and the circumstances of climate and season favouring the development and spread of the two diseases are different, if not opposite—beriberi flourishing under warmth and damp, epidemic dropsy under cold and dryness. Beriberi seems to be a disease of soil and habitation, epidemic dropsy of families or communities—the propagation of the latter being more manifestly due to association and intercourse than that of the former, which seems to depend rather on common exposure to morbific conditions. The diffusibility of epidemic dropsy, though not very active, exceeds that of beriberi, which requires a greater degree of concentration of its poison under circumstances of overcrowding, filth, and deficient ventilation to render it active and effective. The absence of endemic prevalence of beriberi in the localities where the dropsical disease prevailed negatives the idea that the latter was an accidental epidemic manifestation of a malady of usually endemic habit.

Treatment.—Such measures of segregation and disinfection as are ordinarily employed in the case of the exanthems are indicated in the management of an epidemic such as this. No special system or plan of medical treatment or regimen was employed in these outbreaks, symptoms and complications being met by the ordinary principles and methods of rational medicine.

[More detailed information on the subject will be found in the *Transactions of the Epidemiological Society of London*, N.S. vol. xii. p. 55.]

KENNETH MACLEOD.

NEGRO LETHARGY, OR SLEEPING SICKNESS

SYNONYMS—*Maladie du sommeil; Enfermedad del sueno; Nelavane* (Wolofs): *Dadane* (Sereres); *Toruahebue* (Mendehs); *Ntolo* (Congo).

Short Description.—An endemic disease of Western Equatorial Africa characterised by drowsiness, mental and physical lethargy, and progressive muscular debility, which, after a variable period of months or years, generally if not invariably terminates fatally.

History.—It is just a hundred years since the first brief account of this disease was published by Winterbottom. A good deal of information has been gathered since; but there is still much to be learned, not only about the cause and nature of this singular malady, but even about its clinical history, symptomatology, and morbid anatomy, as well as about its local prevalence and the limits of its geographical distribution. The great difficulties attending scientific investigation in the countries in which sleeping sickness is endemic, and the extreme rarity in Europe of imported cases, have hitherto effectually retarded the advance of knowledge of a disease which is of grave importance as concerns the natives of many parts of Africa, and is also of considerable interest to the student of neuro-pathology.

Corre, who personally investigated sleeping sickness in some of its worst haunts in Senegambia, gives us by far the best account of the disease hitherto published; but, as his investigations were carried out some time before many of the more recent and important advances in neurology were made, his account of the symptoms is necessarily not so complete as could be wished. Amongst other original writers on the subject may be mentioned Clarke (1840), who describes the disease as he saw it at Sierra Leone; Nicolas and Guérin, who had large experience among West Indian imported slaves; and Dr. Stephen Mackenzie, who records a case observed very recently in England. Corre and Hirsch give admirable summaries of all that was known on the subject up to the date of the publication of their respective works; to these works the reader is referred for a fuller bibliography.

Geographical Distribution.—So far as known, the endemic area of sleeping sickness is strictly confined to that part of Western Equatorial Africa which lies between and includes the valleys of the Senegal on the north and of the Congo on the south. It has never been known to affect any one who has not at one time or another been resident within this area.

The scanty information formerly available referred principally to places near the coast, but lately we have accounts of the epidemic prevalence of sleeping sickness far in the interior of the continent. It is especially prevalent in the districts of Baol and Sin on the Senegambia coast. It is also found on the Rio Grande, at Sierra Leone, at Cape Mesurado in Liberia, on the Spice Coast, the Ivory Coast, the Gold Coast, at Fernando Po and other islands in the Bight of Biafra, in the Gaboon region, and along the valley of the Ogooué. It is extremely prevalent at many places on the Lower Congo, particularly on the south side of the river, at Mbanza Manteka and Mukimbungu for example; and also somewhat farther south, at San Salvador in Portuguese territory. It seems to be rare or unknown at the mouth of the Congo and at Stanley Pool; but at Lukolula, a place 300 miles above Stanley Pool, it is said to be much dreaded by the natives. Glave remarks of this district that the bitterest malediction one negro can pronounce on another is *Owa na ntolo*—May you die of sleeping sickness.

It would seem probable, therefore, that as our knowledge of Africa extends, this disease will be found endemic here and there throughout the basins of the Senegal, the Niger, the Congo, and their affluents. We have no information of its existence in the districts drained by the Nile and the Zambesi, nor anywhere on the eastern side of the continent.

Its distribution in the endemic area is singularly capricious. It appears to pick out a village here and there, decimating the inhabitants, whilst neighbouring villages may enjoy an absolute or relative immunity. Corre mentions that the garrisons of Joal and Portudal, in Senegambia, are exceedingly liable to the disease, and that when it breaks out in the neighbouring districts the villagers abandon their homes—so great are its ravages, and so much is it dreaded. The Rev. Charles Ingham told me that in the course of four years there were at least 100 deaths from sleeping sickness among the members of the small native church of Mbanza Manteka. The late Dr. Walfrideson informed me by letter, dated from Mukimbungu—a very small village in the same district as Mbanza Manteka—that "several deaths sometimes occur in a week, and that few weeks pass without a death from this cause." Yet in other villages, not very far away, the disease is known only by hearsay. There are also very large districts within the endemic limits where it rarely if ever occurs. Thus Dr. Battersby tells me that he had seen but two cases on the Niger; Dr. Crosse, who has had much experience of the same district, had not seen one case; Dr. Thompstone in eighteen months at Opobo had not seen one; and I have trustworthy information from Old Calabar that there too, though not absolutely unknown, the disease is very rare.

In the days of the slave trade a considerable proportion of the mortality among the slaves during the voyage across the Atlantic was due to sleeping sickness. Moreover, we have indubitable evidence that the liability to the disease persisted after the slaves had landed in America; remaining dormant, as it were, to show itself later, perhaps not until after several years of good health. A case in illustration of this important fact in the natural history of sleeping sickness occurred not very long ago in Britain. A negro lad from the Congo died of the disease at a training school at Colwyn Bay, South Wales. He had lived for three years in this country in good health before the symptoms declared themselves. On the other hand, there is no record of the disease having occurred in negroes born in America, nor in any negro who had not been at one time or another in Africa. Dr. Stephen Mackenzie's case, already alluded to, was imported with the disease fully declared before the patient left Africa. The Africans themselves state that the liability to sleeping sickness persists for at least seven years after the endemic districts have been quitted. Guérin, in an experience of 148 cases at Martinique, never saw the disease in a negro who had not been imported from Africa, nor in one who had been resident on the island for more than ten years.

Local Distribution.—Dr. Walfrideson writes of the disease as he saw it on the Congo. "Several cases have occurred in the same families, and among brothers and sisters. A father or mother may have died from the disease, and one or two of the children have got it after some time. Then there are cases where one or other child is suffering without the parents suffering, and conversely. The more common case seems to be, that the sufferers are picked out singly in families exposed to the same conditions" (private letter). Corre's testimony is to the same effect. The particular and the general distribution appear to be equally capricious.

Age, sex, and occupation seem to have little influence either as regards liability or immunity. Dr. Walfrideson says that he has not seen any baby at the breast suffering from sleeping sickness, but very young children get it. Between the ages of five and fifteen it is fairly common; but in his experience most cases occurred between fifteen and thirty-five. Very old people—that is, above forty (the negro in Africa is not long-lived)—seemed to be exempt. Corre places the period of greatest liability at from the twelfth to the nineteenth year.

Race.—Sleeping sickness is sometimes referred to as a disease peculiar to the negro race. That the negro is more exposed to the cause of sleeping sickness is quite certain, and that he gets it more frequently than any other race is also certain; but that he alone is susceptible is a very different assertion. Corre heard of a case in the person of a European, and he saw it in a Moor. Chassaniol refers to a case occurring in the person of a mulatto. Europeans in Western Africa are so few, and live so much better from a hygienic point of view than the natives, that it is not a matter for surprise that they escape many of the diseases affecting the latter.

Symptoms.—A study of the very confusing and imperfect literature of the subject suggests a division of the disease—somewhat arbitrary, it is true—into three stages, namely, prodromal, declared, and final. The first is characterised by gradually, though intermittingly, increasing drowsiness and muscular feebleness; the second by pronounced somnolence, intense muscular prostration, and, at times, by tremor; the third, in addition to these, by spasmodic contractions of muscular groups, paralysis, bed-sores, wasting, often convulsions, and coma. Mania may supervene at any stage.

The prodromal period is often greatly prolonged; it may continue for months or even for one or two years—some say even longer. At this stage, to the uninitiated, diagnosis may not always be easy. The natives, however, readily recognise the oncoming of the disease, the victim being often the first to foresee the terrible fate in store for himself. We are told that at this stage there is a peculiar puffiness of the face, a suggestive droop of the upper eyelids, a sadness or apathy of expression, and a moroseness of disposition. The patient often feels too languid to work, and is apt to fall asleep at unusual times, even while at work, and in spite of strong efforts to keep awake. He feels cold, and prefers to lie in the burning sun; towards evening there is occasionally a rise in temperature and a quickening of the pulse. Headache and vertigo may be complained of. Occasionally he is seen to stagger in walking, like one half asleep. Gradually—perhaps interrupted with spells of deceptive improvement, or even of apparent recovery, sometimes of months' duration—all these symptoms become intensified; and then the second stage, in which there can be no longer any doubt about the nature of the complaint, is established. The patient is now no more to be found in his usual haunts. He is quite unable to work on account of intense muscular weakness. He takes no interest in his former occupations or amusements, but lies about in his hut or coiled up in a corner of his court asleep, or seemingly asleep with eyes shut or half shut, and absolutely indifferent to everything going on around him. When spoken to, he answers briefly and to the point; but he neither seeks nor encourages conversation. If food be brought he will eat it, although at times the somnolence is so great that he may fall asleep in the act of conveying food to his mouth, or with a half-masticated bolus in his cheek. Muscular tremor is now seen, and it may be severe enough to prevent him from feeding himself. In this condition, if left untended, he would starve. Hitherto he has taken his food sufficiently well to preserve the body in a fair state of nutrition, and the bowels act regularly; but at the final stage wasting of the tissues sets in, diarrhœa may supervene, and, unless carried off by some acute intercurrent affection, he quickly becomes reduced to a skeleton. Enormous bed-sores may form. Choreiform movements or convulsive spasms may affect certain muscular groups, leaving them temporarily or permanently paralysed. Spasm of the pharyngeal muscles, rendering swallowing difficult or impossible, has been noted towards the end. There may also be rigidity of the sterno-mastoids, or of the extensor muscles of the neck. The patient now can hardly be roused. Finally he becomes insensible, and dies either from inanition, or in a comatose state, or in general convulsions.

Such is the ordinary course of a case of sleeping sickness. But it must be understood that there is great variety in the intensity, in the combination, and in the relative preponderance as well as in the course of the various symptoms; no two cases are exactly alike.

Missionaries from the Congo inform me that insanity—often of the nature of religious mania with delusions—occurs in at least 10 per cent of the cases met with there; Dr. Walfrideson says that in some degree it is a common symptom towards the end.

We have no information about the condition of the reflexes except in the case recorded by Mackenzie. In this they were present, perhaps somewhat exaggerated. In the same case the optic discs were examined and found normal, thereby confirming a similar and solitary observation by Sénès (12). The pupil is frequently described as contracted. It is difficult to say whether the droop of the upper eyelids, so constantly referred to by writers, is an expression of simple drowsiness, or whether it depends on a strictly paretic condition of the levator palpebræ superioris. Walfrideson described to me one case in which a staggering gait, with a tendency to fall forward, was a prominent symptom; and there was well-marked lateral nystagmus on looking to the left. Dulling of the sense of touch, complete or partial, in limited patches or in larger areas, is often a notable symptom.

Various curious conditions of the integuments have also been noted. Papulo-vesicular eruptions, attended with intense pruritus, are usual. The eruption is specially common over the front of the chest. Pustular eruptions on the face, according to Corre, are also frequent. Walfrideson mentions cutis anserina as a common symptom, and all writers remark on the scurfiness and lack of the usual velvety lustre of the healthy negro skin. The Rev. W. Holman Bentley, long a missionary on the Congo, and a very close observer, informed me that a sure sign of impending sleeping sickness was a peculiar alteration in the hair; it becomes lighter in the colour, and acquires a reddish tinge; sometimes it turns red. The skin too, he said, puts on a similar reddish tinge.

Enlargement of the lymphatic glands of the neck, apparently not dependent on cutaneous irritation, is said to be another common condition. The glands may be swollen greatly, but usually they do not exceed the size of a small bean. In some localities the natives regard this swelling as the cause of the disease and excise the glands both by way of cure and prevention. The parotid and submaxillary salivary glands also become swollen sometimes, a condition associated with the dribbling from the mouth of a thick glutinous saliva regarded by the natives as infectious.

No particular symptoms have been noted on the side of the thoracic, abdominal, or pelvic viscera.

Pathological Anatomy.—Post-mortem examinations have hitherto yielded very contradictory and indefinite results. States of anæmia, or of hyperæmia of the meninges and brain, as well as softening of parts of the latter, have all been recorded; no constant or characteristic lesion is described. In Mackenzie's case a cysticercus cellulosæ was found on the under surface of the left cerebral lobe; in other respects brain, cord, and meninges, as well as all other organs, seemed to be free from disease.

Etiology and Pathology.—Sleeping sickness has been attributed to such things as sunstroke, beriberi, malaria, poison, peculiar foods—such as raw bitter manioc and diseased grain, excess in venery, palm wine, nostalgia, and so forth; it is evident, however, that none of these things explains all the facts.

The natives of some parts believe that it is hereditary and catching; but the common occurrence of a husband getting the disease, and subsequently the wife, and conversely, is against the former supposition; and the fact that it is never contracted away from the endemic area—in the West Indies, for example, whither sleeping sickness was often imported in the days of the slave trade—is almost conclusive against the latter.

The fact that the disease can be acquired only in a comparatively limited area suggests that the cause is similarly limited; and the fact that the disease may develop years after the endemic area has been quitted suggests that the cause is of such a nature that it may be carried away from the endemic area and remain latent, as regards its disease-producing qualities, for a considerable period; even for years. I have shown in the article on "Worms" that *Filaria perstans*, so far as is known, is limited in geographical distribution to Western Equatorial Africa—that is to say, it can be acquired there only—and that it may continue in active life for many years after its human host has left the country in which alone it can be acquired. We also know that similar entozoa in their wanderings in the tissues, by accident of location, or by disease or injury of their organs, not infrequently give rise to grave lesions in their hosts. I have therefore suggested that possibly *Filaria perstans* may in some way be responsible for sleeping sickness. Such an explanation is compatible with the peculiar endemicity, and also with the peculiar latency of the complaint in some cases. I know that this parasite is extremely common in certain sleeping sickness districts, and, moreover, I have found it in the blood of a considerable number of cases of the disease—in six out of ten —including that described by Mackenzie. There are many difficulties in the way of establishing this hypothesis; of these I am fully aware: but there is sufficient inherent probability about it to make it well worth following up.

Some recent investigations strongly suggest that the particular situation of the primary lesion in sleeping sickness may be the pituitary body. Dr. Lloyd Andriezen, writing on the probable functions of the pituitary gland, and basing his argument on the study of the evolution of this body in the lower animals, says: "The predicable results of the ablation or destruction of the gland would therefore be those due to (*a*) a malassimilation of oxygen by the nervous tissues, and simultaneously (*b*) an insufficient destruction, and therefore accumulation of waste products, thus bringing about a rapid interstitial failure and death of the central nervous system. In general terms we should then expect in the animal: 1. Depression and apathy (the commencing failure of activity in the nerve centres); and, 2, Muscular weakness (the peripheral effect). 3. Loss of fine co-ordination and equilibration (correlated to 1 and 2); and, 4, the development of twitchings and irregular contractions (spasms) of muscles (in relation to the further progress of nutritive failure of nerve centres). 5. A want of sufficient heat production and subnormal temperature. 6. A wasting of body tissues (in relation to the more rapid failure of nutrition of the central nervous system). 7. A probable compensatory polypnœa or attacks of dyspnœa (the peripheral indication of the failure of the nerve centres to absorb oxygen). 8. A rapid progress towards death." With the exception of the last, and of polypnœa, these are remarkably in harmony with the principal symptoms of sleeping sickness; slow incidence of the morbid cause, which we are justified in assuming is the rule in this disease, may explain the very slight discrepancies. Dr. Andriezen's conclusions have been borne out by experimental destruction of the pituitary body by Vassale and Sacchi and by a carefully observed and recorded case of psammoma of that organ by Woollcombe.

Mortality.—The most accurate and trustworthy statistics bearing on this are those by Guérin. Of his 148 cases only one recovered.

Diagnosis.—In consequence of some imperfect observation and ill-considered generalisation by Horton, sleeping sickness has been described by some as a variety of beriberi. A very slight acquaintance with the two diseases suffices to discriminate between them. Sleeping sickness is a disease of the central nervous system; beriberi of the peripheral: beriberi is a disease of rapid development, and recovery is the rule; sleeping sickness progresses very slowly, and is practically always fatal. Beriberi is attended with all the signs of peripheral neuritis, and very generally with more or less œdema; sleeping sickness is not a peripheral neuritis, and is not usually associated with marked œdema; although some puffiness of the face may appear in the earlier stages and œdema of the feet in the later. Sleeping sickness has a very limited endemic distribution, beriberi a very extensive one. Torpor, tremor, insanity, and itching papular eruption are not found in beriberi; muscular atrophy of rapid development, palpitations, abolished knee-jerk, hyperæsthesia of muscles, and many other symptoms characteristic of beriberi, are not found in sleeping sickness.

Treatment.—Temporary relief has followed free purging, large doses of quinine, quinine and iron tonics, and arsenic. The Congo natives administer the juice of *Euphorbia candelabrum*—a drastic cathartic—in the incipient stages. It is to be feared, however, that these measures are of very little permanent service, and that, once established, sleeping sickness must be regarded as being as fatal as hydrophobia.

Mr. Bentley informed me that he believes he once cured a case by large doses of liquor arsenicalis. The patient was his native teacher, at the time twenty years of age. The patient's mother and others of his relatives had died of sleeping sickness. He had suffered from occasional headaches, but otherwise, with the exception of country fevers, was perfectly healthy. He was suddenly attacked with epileptiform convulsions which occurred eleven times in the course of a night. Soon afterwards, or perhaps a little before this occurrence, he suffered from severe occipital headaches every afternoon; the pain was intense, and it seemed to shoot down his spine. He also, from being a bright and lively lad, began to suffer from great drowsiness, so that strong suspicions of incipient sleeping sickness were entertained. He was put on liquor arsenicalis, the dose being gradually raised to eight minims three times a day. After a week's treatment the headaches and the sleepiness left him. Three months later there was a slight relapse, which was also relieved by a course of arsenic. I saw this man five years afterwards in England. He was then in excellent health. I had the curiosity to examine his blood, and had no difficulty in finding in it many specimens of *Filaria perstans*. If *Filaria perstans* be the cause of sleeping sickness, prophylaxis would be concerned with the drinking-water in the endemic area.

Quite recently, I hear, remarkable results have followed hypodermic injections of testicular extract in sleeping sickness; even cures by this means are reported.

PATRICK MANSON.

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P. M.

ORIENTAL SORE

SYNONYMS.—*Oriental boil; Furunculus orientalis; Tropical ulcer; Delhi boil* or *sore; Lahore, Mooltan, Scinde,* or *Kandahar sores; Penjdeh boil, ulcer,* or *sore; Aurungzebe; Lupus endemicus; Caneotica; Clou d'Alep; Clou de Gafsa; Clou du Nil; Biskra bouton; Orient beule; Lib-Lib; Bouton de Crete; Puru* (Malay); *Nisham-al-Tamar* (Baghdad); *Pashsha churdj* (Tashkend).

Definition.—A chronic local contagious disease met with and frequently endemic in certain towns and districts of India, Central Asia, the Levant, Algeria and Malay Peninsula, characterised by the production of small papules which, after assuming the character of a boil, undergo slow ulceration, healing after some length of time with loss of substance, leaving a bluish-white depressed scar.

History.—Although several Oriental medical writers refer to peculiar sores as prevalent in the past in various districts of the East, still this affection had attracted little attention in Europe before the Indian Mutiny in 1857-8, at which time the palace and city of Delhi were occupied by European and native troops. The military cantonment had previously been situated two miles outside the city walls, and the disease was scarcely known amongst the troops; but occasionally cases were met with there, at Lahore also, and at Mooltan. After 1858 the distemper came prominently into notice, as the troops in garrison inside Delhi were attacked with such severity that from 40 to 70 per cent were admitted to hospital suffering from characteristic sores, besides many who were treated out of hospital for similar complaints. The disease was very generally described as tedious and troublesome, though rarely fatal. When severe, or situated on or near a joint, the sores rendered the man unfit for duty; and when occurring on the face were disgusting and disfiguring. In 1865 the Government of India appointed a Commission to investigate the disease. Ten years later a fresh inquiry was conducted by Drs. Lewis and Cunningham on behalf of the Indian Government. Since then a considerable amount of independent literature has accumulated concerning the nature and cause not only of the sores most prevalent at Delhi, but also of those analogous sores known to occur in many localities in different parts of the East. The more recent experiences of the French in Algeria and Tunis, and of the Russians in Central Asia, have again focussed scientific attention upon these sores; and at present by a general consensus of opinion they are all regarded as of the same nature and more or less identical in origin. For this reason it is very convenient to employ some common generic designation, such as that of Oriental sore, suggested by the late Dr. Tilbury Fox. The local names under which these sores are known indicate the places of greatest prevalence; but, speaking generally, they are most common in certain tropical and subtropical climates, from 23° to 45° N. and from 15° W. to 20° E.

Symptoms. — Without any constitutional disturbance, usually the earliest sign of one of these sores is the occurrence of a small inflamed, itching or even burning area on the skin of some exposed part. The skin rapidly becomes boggy and swollen, while in the centre of the inflamed patch a small seed-like body can be felt in the substance of the skin. This hard papule rapidly becomes deep red or purplish in colour, has a smooth and shiny surface, and may vary in diameter from an eighth to half an inch. As the papule increases in size the epidermis covering it shows a tendency to desquamate, the desquamation beginning from five to eight days after the first appearance of the papule. The epidermic scales first shed are fine, glistening, and dry; but as the deeper parts become involved, so the scales become thicker, darker, and moistened by a serous oozing from the surface of the papule: this may be in such excess as to form a small crust. Gradually the papule softens and, if inspected closely, is found to be marked with dilated blood-vessels and several yellowish spots. After a variable time either the scab becomes detached, or the thinned epidermis gives way, leaving a small perforation from which issues a larger or smaller amount of thin purulent fluid. In some cases before the detachment of the crust this may so increase in size and thickness by continual accretion from below as to simulate rupia. The ulceration proceeds rapidly by erosion of the edges, and by the formation of fresh similar papules around it which in course of time break down in the same way, resulting in the coalescence of a number of small sores into one large ulcer with thickened edges and a base of sloughing cellular tissue. The edges are often so much raised as to make the ulcer appear deeper than it really is. The size and shape of these ulcers vary very much; sometimes they may be only half an inch in diameter, in other cases they may be one or more inches across. Usually they are oval in shape, but often present an irregular sinuous outline. The margin is generally ragged, thickened, and surrounded by an inflammatory areola of variable extent. The floor of the ulcer may be smooth, but is commonly uneven, proliferating in one part and disintegrating in another; it secretes a thin offensive pus which, if allowed to dry, forms thick adherent crusts. In some cases the discharge appears so to cling to the sore surface as to form a thick, slough-like yellow pellicle; often yellowish particles, about $\frac{1}{100}$ inch in size, can with a lens be seen distributed on or through the sore; these appear to be degenerated hair follicles or comedones from the sebaceous ducts. The skin in the neighbourhood of the ulcer is generally infiltrated, and marked by small papules and yellow spots, indicative of extension of the disease.

At times these ulcers are extremely painful, while at others pain is completely absent. Ranking and some other writers have noticed a marked tendency to periodicity in the accessions of pain. Although in some cases the adjacent glands may be enlarged, and the lymphatics defined and cordy, the sympathy of the lymphatic system is by no means a constant symptom, and, as Hickman has pointed out, is probably determined by the exact locality of the sores and the amount of irritation to which they are exposed. The ulcerative stage may last for months, the indolent nature of the sore and its intractability to treatment being characteristic. It is, however, in its healing that the oriental sore presents one of its most peculiar features. This process is greatly retarded by the formation of a scaly scab which must be carefully removed each day. Gradually the secretion lessens, the granulations lose their raw appearance, and healing commences from the centre and extends outwards; its course, however, is very slow, the new tissue being very liable to repeat the diseased process—to ulcerate, and start the sore afresh. Cicatrisation ultimately takes place, the scar being more or less puckered towards the centre, and pigmented of an uniform bluish-brown colour. If the attack has been on the face or other part where the cellular tissue is loose, the resulting disfigurement may be severe. The pigmentation of the scars of these sores often remains for years, but is in no way comparable or liable to be confounded with syphilitic pigmentation. In Baghdad the scars from these sores are known as "date marks."

The number and locality of the sores vary. Some patients may have but one or two; others may have as many as twenty: when multiple, the individual sores are often not so large as when single, and are said by some observers to be less intractable. The disease is most commonly seen on exposed parts, such as the hands, arms, feet, legs, neck or face; in children the face is the usual situation. It is very liable to attack abraded surfaces, wounds and scratches. Insect bites are very often the starting-points for them. In my own experience, the dorsal surfaces of the wrist and borders of the forearms are the points most frequently attacked. The noses of dogs have been observed by many persons to be the seat of these sores, which they apparently contract when drinking.

The appearance of this disease is not always uniform; it may stop at any phase, and it may assume a chronic character when in the papular or boil-like stage, gradually subsiding and disappearing. In other cases, even after the formation of a crust, this may not fall off, but persist until cicatrisation is complete beneath it; or sometimes the ulcerative process may be so vigorous and involve fresh tissues so rapidly, as closely to resemble *lupus exedens.* Some sores may become extremely inflamed from friction of clothes or other irritation: occasionally complications arise from inoculation with the virus of erysipelas or of phagedæna; this is, however, rare. When the sores occur on the persons of the scrofulous or syphilitic their clinical features are frequently modified. Any disadvantage arising from starvation, overwork, malaria, or the syphilitic and scrofulous cachexies will modify the type of the sore and accentuate its intractability; but such constitutional or hereditary conditions do not necessarily dispose to the disease. In extreme and most exceptional cases, where the patient is weakened by constitutional disease, or the sores are multiple, the resulting discharges and irritation may be very depressing and be accompanied by hectic fever.

Diagnosis.—In districts where the disease is known to be endemic this should not be difficult; as the appearance upon the face or other exposed part of an isolated papule, developing into a nodule, and this exuding, crusting, and then disintegrating into an obstinate ulcer under the crust, constitutes a distinctive set of symptoms. In some cases it might be mistaken for a syphilitic gumma or rupia, but the failure of specific remedies and the general clinical conditions should indicate a differential diagnosis. Although it has been confounded with ecthyma and impetigo this mistake should not readily occur. When present in a severe form upon the face there may be more difficulty in disassociating it from rodent ulcer, lupus, or epithelial cancer.

From yaws it can be readily distinguished by remembering that yaws is almost limited to the coloured or negro races, while oriental sore attacks all races alike. Yaws is preceded by some febrile symptoms;

these are rare in the sore. In yaws the lesions are always multiple or numerous, coming in crops; the boil or sore is usually single, and if multiple not numerous. Although both attack the face, yet yaws prefers the flexor surfaces, such as the palms and soles; whereas the boil prefers the dorsal aspects of the hands and feet. In both affections the lesion is that of a papule succeeded by a nodule; but in yaws the epidermis splits off in a few days, and the whole eruption is developed in a few weeks: on the other hand, the nodule of oriental sore may remain unchanged for months. When the crust of the yaw papule is removed only a moist tumour is found which, except in the very cachectic or when irritated, never ulcerates; when the crust of the oriental sore is removed an ulcer is exposed. Yaws leaves no scar, but oriental sore necessarily does so.

Malignant pustule, or external anthrax, can be readily distinguished from oriental sore by its size and extent of swelling, by its tendency to spread, by the livid tint of the skin and the early formation within it of more than one aperture, by the character of the slough, by the severity of the pain, and the marked constitutional disturbance; to this may be added the discovery of the specific bacilli of anthrax.

Pathology.—The histology of these sores has been thoroughly worked out; and, if sections be made of the initial papule before ulceration, no difficulty is experienced in demonstrating that the whole thickness of the skin and subjacent tissue is infiltrated with lymphoid and epithelioid (mesoblastic) cells, accompanied by more or less complete disintegration of the normal tissue elements thereby. In the centre of the papule the infiltration by young round cells is so complete that little can be seen of the original tissue elements but a few degenerated remains of hair follicles or sweat glands. Towards the edges of the diseased area the new cells occur in isolated clusters or groups, chiefly round blood-vessels or lymphatics. The infiltration does not seem primarily to involve either the hair follicles or the sebaceous glands. The individual cells of this infiltration vary from $7\ \mu$ to $9\ \mu$; their nuclei from $3\ \mu$ to $6\ \mu$: the nuclei are large, generally single, but in parts multiple. The anatomical structure of the papule and surrounding skin indicates that oriental sore is of the type of a granulation tumour.

All authorities are agreed on this general statement of the histological changes met with in oriental sore; but when we come to inquire into the causation of this peculiar process, we find some divergence both of opinion and of facts.

The first precise inquiries in this direction were made by Fleming and Smith in 1868. The former found in the diseased tissues certain small, highly-refractive cells, which he took to be the eggs of a parasite; these were subsequently demonstrated to be disintegrated hair follicles: later, Smith found in the pus from the sores cells of various sizes and forms which he thought were ova, or, at least, larvæ of a species of distomum. Both these observations were obviously founded on error due to the imperfect means of investigation available at that time. In 1875, Vandyke Carter, in examining specimens of a "bouton" sent to him by

Weber of Biskra, believed he found in the dilated lymphatic vessels a filamentous mould, with mycelial threads and gonidia. In these observations Weber concurred, but further investigations by Laveran and Kelsch demonstrated that the presence of these bodies was entirely accidental or adventitious. In 1880, Bordier, a French naval surgeon, described very similar growths. Lewis and Cunningham, in their report upon Delhi sore, dated 1876, and Geber of Vienna in discussing Aleppo evil, infer the identity of these oriental sores with lupus, and disclaim any ability to find histological features in them at all suggestive of their being peculiar diseases.

The researches of recent years, conducted with a higher technique, have yielded more definite results. MM. Boinet and Dupéret, from some Algerian cases of the disease, have obtained pure cultures of micrococci which, according to these observers, produce on inoculation characteristic oriental sores. M. Duclaux, in Paris, has also reported the isolation of a micrococcus from a case of "clou de Biskra." His results agree with those of Heydenreich of St. Petersburg, who has examined specimens from Penjdeh; but with some minor differences which suggest a doubt whether this micrococcus is exactly the same as that of Boinet and Dupéret. Still later, M. Gessard, a French surgeon-major at Gafsa, has obtained a micrococcus from some ulcers prevalent there which Duclaux regards as identical with that noted by him in a sore from Biskra. Chantemesse obtained very similar results from a case of "clou du Nil." Poncet, working upon another case from Gafsa, states that he has discovered not only micrococci, disposed in zooglœa masses between the epithelial cells, but also some bacilli. Riehl, of Vienna, has also detected micrococci in a papule from Aleppo. As described by him they are somewhat larger than those found by the French observers Duclaux, Boinet, Dupéret, Gessard, Chantemesse and Poncet; being in one case from 0·9 μ to 1·1 μ, and in the others from 0·25 μ to 0·5 μ in size. Riehl finds the micrococci in the large epithelial cells and also in the large polynuclear cells; they appear to have a capsule and are slightly oval: so far he has failed to cultivate this organism. Cunningham has described refractile bodies larger than lymph corpuscles in the tissues of the papular stage of these sores. They appear to be cells from 8 μ to 10 μ in size, enclosing certain round and deeply-stained bodies of variable size and grouping. Cunningham is inclined to regard them as representing various stages of some monadinic organism. From an examination of various papules of the Lahore, Mooltan and Scinde sores, removed before ulceration, I can confirm the presence of the cellular bodies described by Cunningham, but am disposed rather to regard them as results of some degenerative process in the cells than as parasitic protozoa. Although I have not been able to isolate any definite micro-organism from the tissues of these sores which, on inoculation, will give rise to similar ulcers, still there is usually no difficulty in cultivating large micrococci from them, and in demonstrating that the epithelial cells consistently contain peculiar bodies which are highly suggestive of such parasiticism.

The manipulations which most clearly show the microscopical characters of these cells may be described as follows:—Place the fresh tissue in a saturated solution of corrosive sublimate and then harden successively in 30, 60, 90 per cent, and finally in absolute alcohol. After embedding in paraffin, pass the sections through tincture of iodine in order to remove the excess of sublimate. Stain with hæmatoxylin, or with carmine and lichtgrün, or with the Ehrlich-Biondi mixture, or any other staining reagent. When so examined, the parasite-like bodies in question are seen as small round elements, which sometimes appear to have a more darkly staining centre, generally lying in the protoplasm of an epithelial cell. In size these bodies are about 0·5 μ to 1 μ; they stain easily both with protoplasmic and nuclear dyes, but have a slight preference for the former, as, if lichtgrün be used as a counter stain, they retain it after all traces of the stain have left the nuclei of the cells. Similarly, with Biondi's mixture, they stain red with the acid fuchsine, showing at the same time a central green part. These cocci are to be seen in the large polynuclear, as well as in the epithelial cells; but I have never yet satisfied myself that they are capable either of movement or of division. Owing to the number of leucocytes and degenerated epithelial cells which always obscure the picture of sections of these papules, it is often difficult to recognise these bodies with certainty. They conform in size and locality to the micrococci described by Riehl, and are quite distinct from the much larger or polynuclear cell-like bodies noted by Cunningham. There is nothing in the above-mentioned bodies to exclude the possibility of their being due to some form of cell degeneration. On the other hand, there is much in their general appearance and location to suggest that they are intracellular parasites. If parasitic it is necessary to inquire to what group of organisms they may belong. The chief groups of unicellular parasites which pass part of their existence within the cells of their host are the chytridiaceæ, some of the suctoria, and the sporozoa. The few features already observed do not suffice to refer these bodies to any of these classes. Arguing from their close resemblance to other bodies found in cancer, sarcoma, variola and vaccinia, we may tentatively regard them as sporozoa.

The want of uniformity in these various results, as reported by different observers, prevents our saying more than that in all cases of oriental sore, and especially in the epithelial cells, certain coccoid bodies are met with, which are sufficiently definite to warrant the belief that they stand in direct causal relation to the morbid process.

Etiology.—No age, sex, nationality or occupation modifies liability to attack in those who fall within the influence of this disease. In endemic localities children rarely escape. Some authors, particularly those whose experience has been in Persia, state that new arrivals are especially prone to attack; this feature has not been very generally recognised by Anglo-Indians. The *period of incubation* is variable, but usually some weeks elapse between exposure to the disease and development of the papules. As a rule new arrivals do not get it until they have resided some time in the district, but cases are on record of a few days being sufficient. In other instances the affection has not appeared until the individuals had left the locality. In some cases inoculated by Weber the incubation period was as short as three days. The affection appears to be quite independent of the nature of the soil; but its peculiarly definite geographical limitations indicate the influence of tropical and subtropical climates.

As bearing upon the possibility of one attack of these sores being a protection against a second, Colvill, quoted by Carter, states that at one time it was the custom in Baghdad to inoculate children with these sores so as to ensure the disease in a situation where the resulting scar would not be disfiguring. On the other hand, Murray and Fleming found that the sores could be successfully inoculated upon persons showing scars of a previous attack. Similar results are recorded by Boinet and Dupéret, who have definitely proved that it is inoculable both in men and animals, notwithstanding previous attacks. They have also demonstrated the possibility of auto-inoculation. The occurrence of personal contagion from these sores appears to be very rare; and there is no evidence of hereditary influence. More recently Heydenreich has proved the communicability of the disease by direct inoculation. According to him infection is without difficulty produced by rubbing the powdered crusts or the blood and lymph from non-ulcerated papules on abraded surfaces. The seasonal prevalence of these sores is chiefly in the latter part of the summer and in the autumn, that is, in subtropical climates, in August, September, October and November; and in the first part of the cold season in the tropics.

In attempting to determine more precisely the causes of these sores we find:—(i.) that the disease is limited to certain places; (ii.) that healthy as well as weakly people are attacked; (iii.) that the disease can be conveyed by inoculation. The first two propositions point strongly away from constitutional causes, and rather to some local conditions of soil, insanitation, or water which favour the multiplication of the morbific agent outside the human body; while the third suggests that this agent, whatever it may be, is an organism. The very general occurrence of these sores on those parts of the body which are exposed at once suggests that the inoculation or infection may be effected by insects such as mosquitoes or flies; or again by dust or some accidental application of the virus to an abraded surface. In explanation of the excessive prevalence of these sores on the faces of young children, Laveran has pointed out that this is in them the most exposed part, and that they are less quick to brush away any insect which may be biting them.

The sores are equally prevalent upon wet soil or dry, on rock or sand, in high situations or low. It is difficult to show that the endemic areas of the disease are areas of overcrowding, of accumulated refuse and excreta, or even of faulty alimentation; or that these sores are but the expression of a depraved nutrition from climatic or other unhealthy influences. The great diminution in the number of cases of this affection which has followed ameliorated sanitary conditions of towns and districts where formerly it was very prevalent lends some support to such an opinion; yet in the experience of many observers, including my own, these cases occur in camps and cantonments in which there is neither overcrowding nor defective hygiene, and also on persons free from any cachectic condition of body produced by unhealthy climate or otherwise.

Nearly all observers have attributed the origin of the oriental sore to the domestic water-supply, though they have not been equally unanimous in indicating the injurious element. Some French writers have attached importance to an excess of chloride of sodium and of the earthy salts; others have laid stress upon the disposing influence of large quantities of sulphate of lime in the streams of endemic areas. Candy and Fraser pointed out the excess of nitrates in the wells where Mooltan and Lahore sores prevailed, while Alcock was inclined to blame the presence of sulphuretted hydrogen, resulting from the decomposition of organic matter in the water. Lewis and Cunningham suggested that excessive hardness may be an index of the deleterious property of drinking-waters which in various parts of India are associated with the prevalence of the sores. It is true that in Delhi and elsewhere, since the disuse of the water from wells within the city, the disease among British troops has abated; but the existence of similar chemical defects in the drinking-water of many other places where the disease is unknown make this opinion impossible. In Algeria and Central Asia various impurities in food and drink, and the blocking up of the sudoriparous glands with dust, have been respectively assigned as active causes of this affection. If we admit that the water-supply is the vehicle by which the agent gains access to our bodies, the question arises whether it is taken into the system by swallowing, or whether it passes into the skin through the gland ducts or by abraded surfaces when washing. Against the acceptance of the drinking-water hypothesis is the fact that many places where exceptionally good drinking-water is in use are endemic centres of the sores. As Hirsch has pointed out, if this hypothesis were true, it would be difficult to explain why these sores have certain points of election in the body, such as the face and exposed parts of the extremities, and occur very rarely on the trunk; or why persons are continually affected with these sores who are only acquainted with the internal uses of water. If the domestic water-supply be concerned in the production of these sores and ulcers, it is, as suggested by Murray and others, by reason of its containing some specific or parasitic body which finds attachment to the skin when the water is used for washing, and either spontaneously penetrates the cuticle, or else obtains entrance by some solution of continuity, such as a scratch, cut or abrasion. Notwithstanding that the actual cause of these sores has not been categorically defined, still the weight of evidence is in favour of its parasitic nature. It is to be regretted that more extended and close inquiries have not been made into the fauna and flora of the sources of water, particularly of wells, in districts where these sores are prevalent. In discussing this subject recently with various medical officers of Indian experience, my attention was drawn to the more frequent association of these sores with the use of old and foul wells than with canal supplies. It is probable that investigations in this direction may supply the missing links of the chain of evidence concerning the life-history of the micro-organism which appears to be associated with the causation of this disease.

Treatment.—Some authorities have advocated what is called the abortive treatment of these sores when in the early or papular stage. This needs some care and much personal supervision to be successful, and is best carried out by the application of Pacquelin's or the actual cautery. The use of carbolic and other acids is not to be recommended, nor is excision. When ulceration has been thoroughly established, the use of caustic potash, nitric acid, fuming acid, nitrate of mercury or carbolic acid is valuable, but inferior to the judicious use of a Volkmann's spoon. For the removal of crusts antiseptic poultices may be applied; but in all dressings the greatest cleanliness should be observed and all irritative treatment avoided. Once the diseased process has been checked and the ulcer has taken on healthy action, the ordinary treatment for simple ulcers is sufficient. As many of the sufferers from these sores become rapidly debilitated in general health, care should be taken to supplement local treatment by a generous diet including wine or beer. Any evidence of malaria, scurvy, scrofula or syphilis should be met by appropriate treatment. In cases occurring in India I have generally found it necessary to remove the patient from the endemic areas; preferably by change to the hills. It is perhaps needless to say that in places where the sores are prevalent it is of the first importance to avoid the use of water, which may be infected, either for washing or drinking, unless previously boiled.

R. H. Firth.

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R. H. F.

VERRUGA

Short Description.—A chronic infectious febrile disease, prevalent in certain narrow steep-sided and confined valleys on the western slopes of the Andes, characterised by an irregular prolonged and often intermittent febrile condition, with anæmia, followed sooner or later by the appearance of red tubercles of variable size on the cutaneous surface of the body.

History.—On the west coast of South America the disease is known under the names of Peruvian Wart, Verruga Peruana, Verruca Andicola, and Fiebre de la Oroya. It appears to be peculiar to Peru, being endemic in certain Cis-Andean localities, more especially in Huarochiri and Yauyos y Canta, at an elevation of from 3000 to 8000 feet above the sea-level.

The disease seems to have attracted attention from the earliest times, having been known in the days of the Incas. It was referred to as early as 1543 by Augustin Zarate in his History of Peru, in which he mentions a tract of country which "is very hot and unhealthy, the inhabitants suffering particularly from very malignant pimples (verrugas) or furuncles with deep roots, more dangerous than small-pox and almost as much so as the carbuncles of plague." The affection is also mentioned by Cosme Bueno in his *Descriptiones Geograficas*, and by Tschudi in his work on Peru, dated 1843. The first scientific description of the disease was given by Salazar in a graduation thesis delivered at Lima in 1858, entitled *Historia de la Verrugas*, in which he clearly demonstrated it to be an endemic disease due to a poisonous virus. Since then numerous accounts of cases have appeared, by Dounon, Fournier, Bourse and Tupper, chiefly based upon the outbreak of the disease in 1870 and following years among those employed in constructing the railway from Lima to Chicla, on the road to Oroya. A disease apparently identical with verrugas has been recently reported by de Havilland Hall as being prevalent at Zaruma in Ecuador.

Symptoms.—There are practically three stages in this disease. First, one of incubation, lasting from fourteen to forty days, without any definite symptoms; second, a period of invasion and fever, followed by a third stage of eruption and convalescence.

The onset of the disease is marked by malaise, languor, headache, fever and considerable gastric disturbance. The fever is usually irregular, and in many cases indistinguishable from a malarial intermittent, having daily cold, hot and sweating stages. In some cases the fever is remittent. A characteristic and early symptom is the presence of dysphagia with cramp-like pains in the muscles. These muscular pains are often excruciating at night, being associated not infrequently with inflammatory swellings of the joints. The osteocopic and myalgic pains are agonising at times and comparable with nothing experienced in other diseases. Accompanying these symptoms there is often a progressive anæmia, with œdema of the extremities, marked debility, and some tenderness or enlargement of the spleen and liver.

After these symptoms have lasted from one to nine months or a year they gradually remit or vanish with the appearance of a characteristic eruption, which consists either of raised spots about the size of a pea, which develop into cylindrical, conical or hemispherical tumours, varying in size from a raspberry to that of a pigeon's egg; or of minute, hard, movable subcutaneous tumours, which may either disappear or increase in size into dusky red, shining and itchy tumours.

The first variety of lesions are very vascular, itch, and, if scratched, bleed freely; ultimately they crust over and heal. If uninjured the warty growths remain stationary some time, darken, and slowly subside, leaving after desquamation a discoloured area which eventually disappears, leaving no scar whatever.

In the case of the subcutaneous tumours the skin over them often gives way, and the morbid growths appear as fungating, fleshy swellings of a gray or black colour exuding an offensive sanguineous secretion. The size of these warty growths may vary from that of a pea to that of an orange, being in shape sometimes pedunculated like a mushroom, or again sessile and hemispherical. Not infrequently abscesses may form before the subcutaneous tumours break through the skin; or, after rupture of the skin, ulceration may ensue, in this case they may become encrusted and rupial in character. The essential feature of all these eruptions is their vascularity; the warts either bleed spontaneously or on the slightest provocation, draining the already anæmic and debilitated patient.

The eruption is usually most abundant on the face and extensor surfaces of the extremities, especially on the knees, elbows and malleoli. The trunk is less usually attacked. The number of excrescences varies from one to several hundred of all sizes and shapes. These tumours may also form on the conjunctivæ, in the nostrils, on the tongue, the mucous membrane of the pharynx, glottis, alimentary canal, and internal viscera. In these situations they may give rise to symptoms not only anomalous, but grave; such as hæmorrhages, suffocation, dysphagia and ascites.

The disease generally lasts two or three months, or even longer; but not infrequently it is fatal earlier from hæmorrhages. In cases which survive there is usually profound anæmia, dropsy, or affections of the nervous system. The mortality among the indigenous populations of endemic areas is about 10 per cent—in whites rather higher; and in epidemics may amount to as much as 40 per cent. Cold has an unfavourable effect upon the eruption, causing it to be imperfectly developed, with an aggravation of the constitutional symptoms; while a diminished barometric pressure favours hæmorrhage. Consequently verruga cases do better in warm places and at sea-level than in cold and elevated situations. This fact largely explains the greater fatality experienced in some outbreaks as compared with others, the mortality being apparently related and in proportion to the lowering of the atmospheric temperature and pressure. Apart from hæmorrhages, considerable danger exists among the very poor and indigent from septic absorption in connection with their unhealthy and often very extensive sores.

Pathology.—If sections be made of the tumours, they are found to consist primarily of a delicate fibrous stroma, the meshes of which are filled with round cells, the whole being enclosed in a sort of fibrous capsule. The smaller growths appear to spring from the papillary layer of the skin; the larger ones arise from the subcutaneous tissues. All the tumours are extremely vascular, the larger ones presenting in their centre cavernous spaces filled with blood. In some severe cases these vascular and warty growths are found after death not only on the skin but upon the mucous linings of the stomach and bladder, or even on the upper surface of the liver. Both this latter organ and the spleen are generally also much enlarged; but beyond these lesions on the viscera and skin, there are no evidences of great pathological changes.

Isquierdo has described a bacterium which he found in the morbid growths in some profusion. From his account this micro-organism appears to be from 7 μ to 10 μ long, beaded, and somewhat larger than the bacillus of tubercle. The capillaries are often distended or varicose, being filled with microbes which are also occasionally met with in the vessels of the adjacent and apparently healthy skin. Isquierdo's accounts of these organisms are not very precise; nor does he appear to have made satisfactory culture experiments to indicate their specific relation to this disease.

Etiology.—Imperfectly as the pathology of this affection is worked out, it is not surprising to find its etiology still shrouded in some obscurity. From a somewhat extensive knowledge of the countries on the western coast of South America, I am disposed to believe that the distribution of this affection is by no means confined to either Peru or Ecuador, but that it is endemic also in Bolivia and the northern parts of Chili.

Neither age, sex, nor race has any influence upon verruga. That the disease is inoculable was demonstrated by the fatal experiment of Daniel Carrion, a young student in Lima, who, in order to elucidate the disease, inoculated himself with the blood of one of the warty growths; his death may possibly, however, have been due to septic infection. The disease cannot be regarded as contagious, as patients suffering from verruga, even when treated in general wards, do not communicate the affection to others. A popular opinion prevails in Peru that one attack can confer immunity against subsequent attacks. It is extremely doubtful whether the facts justify this view; certainly, so far as my experience goes they do not. I met with several cases, both at Surco and Matucana in Peru, in persons who assured me that they had had the disease some years before, and had in the meanwhile remained quite free from all symptoms.

The disease is undoubtedly endemic in certain well-defined areas, and the native belief is that the affection is contracted by drinking water from particular springs and streams. Prolonged residence in the endemic districts is certainly not necessary to contract the disease; but, on the other hand, notwithstanding Dounon's statements to the contrary, a mere passage through the country, without either eating or drinking on the journey, or being thrown in intimate contact with the inhabitants, is not sufficient to produce it. It is difficult to eliminate the water-supply as a possible etiological factor in a country where sanitary arrangements are, at the best, very unsatisfactory; but a close inquiry into the circumstances and occupations of a large number of verruga patients convinced me that the disease occurs only in those brought into intimate contact with the soil, notably those engaged in work which necessitates the handling of mud or earth; such as mining, tunnelling, and agricultural employments, particularly upon rice fields and tea or coffee plantations. This point has hitherto been overlooked by previous observers, and remembering the fact that large numbers of the inhabitants of these verruga districts are the subjects not only of filariasis, but of helminthiasis generally, it is not improbable that the true solution of the pathology and etiology of this affection will be found in the association of the disease with some form of parasitic worm, whose free stage is passed either in water or mud, most likely in mud. I would strongly urge that future investigations into the etiology of verruga should be directed on these lines—more especially to the determination of the presence or absence of some form of hæmatozoon either in the warty growths or in the tissues generally of the affected person.

That verruga has anything in common with malaria does not merit serious discussion; it is true the fever of verruga may occasionally be very like malarial fever in form, but this is simply due to the fact that the majority of those suffering from verruga are also the subjects of chronic malaria; and the fever thus complicated may assume an intermittent or even a remittent type. Malaria is exceedingly common in the Andean valleys, but it is in a few of these valleys only that verruga is found.

Treatment.—The first essential in the successful treatment of this affection is to remove the patient out of the endemic area, and to transfer him, if possible, to a warm region at or near the sea-level. There is no known specific for the disease. All that can be done is to maintain the strength of the patient on general principles by a suitable and generous diet, combined with attention to the cleanliness and asepsis of the skin. Sloughing warts should be removed and ulcers treated by ordinary methods. As hæmorrhages are the most dangerous complication in this disease, styptics and compresses should always be kept available for sudden emergencies. Many of the fatal cases among the coolies and others suffering from verruga in out-of-the-way valleys arise from imperfect methods and facilities for guarding against profuse loss of blood. Transfusion or saline injections are by no means uncalled for. During the eruptive and convalescent stages both iron and arsenic, with other tonics, are naturally of the greatest value; but at best the treatment of this disease is empirical and unsatisfactory, and so must remain until its etiology and pathology are better understood.

R. H. FIRTH.

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R. H. F.

FRAMBŒSIA

SYNONYMS.—The name Frambœsia was originally given to this disease by Sauvages in 1759, from the French word *framboise*, a raspberry, because of the resemblance of the characteristic growths on the skin to that fruit. In the West Indies the colloquial name for it is *yaws*, possibly from the native word meaning a strawberry.[1] Similarly, in the French Antilles it is called *pian;* in the Brazils, *boba;* on the West African coast, *gattu*, *dubé*, and *tangara;* in the Moluccas, *bouton d'amboine;* in Fiji, *coko;* in New Caledonia and the Samoan Islands, *tonga* or *tono;* and in Ceylon, *parangi*.

Short Description.—A chronic, specific and contagious disease, characterised by an eruption of raspberry-like tubercles, usually accompanied by more or less constitutional disturbance, and tending slowly to spontaneous cure.

Distribution.—Frambœsia is essentially a disease of tropical climates, being found chiefly in Dominica and Jamaica in the West Indies; on the West Coast of Africa for about 10° on each side of the Equator; in Madagascar and Mozambique; in Oceania, chiefly in Fiji, New Caledonia, and Samoa; in tropical South America; in Ceylon, Java, and Sumatra; and less commonly in Assam and some parts of India.

History.—Although Ali Abbas, an Arabian physician writing in 977, mentions a disease under the name of "safat" which may possibly have been frambœsia, our first reliable accounts of the affection are by Oviedo, who met with it in St. Domingo, and writes of it under the name "bubas." Subsequently, in the seventeenth century, we find various medical accounts of it from the Brazils and the West Indies, by Piso, Bontius, and Labat; a hundred years later, Sauvages recalled attention to it in his classical work *Nosologia methodica.* It is, however, chiefly to Gavin Milroy, Murray, Bowerbank, Macgregor, Charlouis, Kynsey, and other observers of the last twenty years, that we owe most of our present knowledge of it. As in the case of most other diseases, we have no very precise knowledge how this peculiar affection originated; but sufficient is known to justify our belief that, so far as its prevalence in the West Indies is concerned, the original habitat of frambœsia was the West Coast of

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[1] Nicholls has suggested that the Celtic word *ias*, pronounced *yas* and meaning heat, boiling or bubbling up, is the true source of the English derivation of the name yaws.

Africa, whence it spread by the exportation of negro slaves to the Spanish Indies. On the other hand, there is evidence to show that, notwithstanding an extensive negro immigration, many regions of the tropics have been free from yaws; and that it has raged in the past, or exists now in other parts of the world, such as Polynesia, whither no importation of negroes has taken place.

During the period of slavery the disease appears to have prevailed with some virulence in the West Indies, where special means had to be adopted for the isolation and treatment of those affected. In some islands, notably in Dominica, after the abolition of slavery the disease largely increased; owing apparently to the lessened supervision which the authorities were able to exercise over the housing and general condition of the negroes. In Jamaica, on the other hand, Bowerbank relates that a diminution took place after the emancipation; this he attributed to the cessation of the practice of inoculation which previously had been prevalent among negroes. In recent years several recrudescences of the disease have taken place, while Antigua and Barbadoes are now practically free from the affection. It is still met with on the West African coast, and last year was observed in Assam.

Symptoms.—There are practically four stages in this disease: First, one of incubation, lasting from two to seven weeks without any very special symptoms; second, a period marked by a febrile condition which lasts from two to eight days, terminating usually with the appearance of an eruption; third, a period marked by successive crops of the eruption, which may last from a few months to two years; and, fourth, a lengthened period of sequels, often extending over five or seven years.

The *incubation period* is difficult to determine, and has been variously stated by different observers. Paulet, who inoculated healthy negroes with yaws fluid, puts it down from ten to twenty days; but extensive clinical experience indicates that it varies from a fortnight to two months.

Premonitory Stage.—During this period there may be no disturbance of health; but not infrequently there are vague pains in the limbs, palpitation, indigestion, and even fever. These constitutional disturbances are usually more marked in children than in adults. In negroes the skin commonly loses its lustre, becoming scaly and often lighter in colour. These symptoms often remit before the appearance of the eruption, which occurs in from seven to ten days, and is preceded by enlargement and tenderness of the lymphatic glands. At this time, if a case be closely examined, the seat of inoculation may perhaps be discovered as a minute papule exuding a pale yellow fluid, or even as a very slight growth of granulation tissue. But more commonly, in spite of careful search, no lesion indicative of the point of entrance of the poison is to be found. If by chance framboesia virus happens to have gained access to the body through an existing ulcer, this will be noticed to have retrograded and become unhealthy-looking.

Eruptive Stage.—The eruption makes its appearance as a small papule, usually, but not necessarily, on the scar of an old wound or sore, giving a clue to the seat of inoculation. More often it consists of slightly elevated papules about the size of a pin's head, single or scattered over the body, and having a broad base; if situated on the lips it looks like a commencing herpes. In a few days the papules enlarge, forming tubercles varying from a quarter of an inch to two inches in diameter. As the papule increases the epidermis splits or cracks, exposing a raw papillary surface from which oozes a yellowish-white sero-purulent fluid. Unless irritated these tubercles do not resemble the raspberry. The yaws are usually circular in form, and may be met with of all sizes on the same patient, varying from a pin's head to that of a golf ball or even larger, and in every stage of progress. Generally they are discrete; but sometimes one sees them in groups, or arranged in a circle enclosing healthy skin. This variety is sometimes spoken of as "ringworm yaws."

Imray has described two unusual forms of the eruption. In one the tubercles are replaced by circular scurfy areas of different sizes. These are known, among the negroes, as *dartres*, and are very persistent and rebellious to treatment. The other variety appears as small, slightly prominent vesicles distributed over the body, called *pian gratelle;* they frequently follow an ordinary eruption of frambœsia, and are also very difficult to cure.

When the disease attacks the soles of the feet or the palms of the hands it is called *tubbæ* or "crab yaws." The epidermis being usually very thick in these situations the yaws are unable to expand, and thus give rise to much pain. When they do break through, the resulting growth is often small, but secretes an abundant serous fluid. Sometimes these cases present a honeycombed appearance from the excess of exudation and the thickening of the cuticle around the openings.

In some rare instances one of the frambœsia tubercles may assume very large proportions—one or two inches in diameter—projecting from the skin like the other yaws, and covered with yellow scabs. Such a tubercle receives the name, among the English, of "mother yaw"; and in the French patois of some West Indian islands is called a "maman pian." While all the smaller yaws may entirely disappear this large one may remain, and, if neglected, ulcerate, eating its way into the tissues, causing extensive and often irreparable destruction of the soft parts, and setting up extreme constitutional irritation and emaciation.

The simplest and most ordinary tubercles of frambœsia do not usually ulcerate; but, attaining a certain size, form a yellow scab, shrink, and finally, on the crust falling off, leave purplish-blue spots. In some instances the scabs form to such an extent as to produce crusts closely resembling rupia; if the scab be removed the surface left is commonly bright red in colour, and not at all unlike a raspberry; but in old and asthenic cases the secreting surface is a dull yellowish white. When the yaws are in moist situations, as round the mouth, nostrils, or anus, on the perineum, or in the folds of the thighs and nates, crusts do not form; the lesion then closely resembles a syphilitic mucous tubercle. Unless on some very exposed part, or when ulcerated, the tumours are not very sensitive;

they often itch and emit a curious musty and offensive smell. The yaws tubercles are relatively rare on the scalp and trunk, but are most frequent on the face at the corners of the mouth and nostrils, on the neck, arms, axillæ, legs, thighs, buttocks and vulva.

The constitutional disturbance during this eruptive stage is variable; frequently the patient has a good appetite, is able to move about, and, excepting the presence of the yaws, is apparently in good health: in other cases there are distinct fever, muscular pains, occasionally cramps, loss of appetite, debility and anæmia. The eruption may last from a couple of months to a couple of years, successive crops of tubercles coming out at intervals; but the duration largely depends upon treatment, food and hygienic conditions. Occasionally one or two tubercles may appear some length of time after every symptom of the disease has disappeared. How far these are recrudescences of the original disease, or the effect of a reinfection, is at present uncertain; probably the latter is the case.

The most characteristic features of yaws are that, unless pressed firmly, they are not tender; and they do not degenerate and ulcerate except under irritation, bad treatment, and enfeebled general health. Their general tendency is to cure, gradually shrivelling up and falling off, and leaving a pigmented spot which eventually disappears. The lymphatic enlargement, which in some cases may be extreme, invariably subsides as involution begins. With the disappearance of the eruption the general health recovers; and in ordinary cases no after-effects are experienced. All cases, however, do not terminate in this favourable manner; particularly is this the case if the patient be unable to get good food, be scrofulous and debilitated, or be placed in unfavourable conditions. In these cases, instead of the tubercles gradually disappearing, they ulcerate freely, involve deep parts, and, if death do not in the meantime occur from exhaustion, pyæmia or septicæmia, they heal slowly, leaving irregular and extensive cicatrices. It is not uncommon in the West Indies to see men and women helpless cripples, as the result of contractions and stiffened joints following the healing of these ulcers. In the more severe cases gangrene of the toes and feet has been known to follow; while in rarer instances ulceration of the nasal bones has been seen. These severe cases were much more prevalent in the past than now, and were probably due to imperfect methods of treatment—more especially to the abuse of mercury. Except in these extreme circumstances, the internal organs are unaffected; few cases are fatal if properly treated.

Diagnosis.—The presence of initial papules, which enlarge to tubercles over which the epidermis splits, leaving bare a raspberry-like tumour which remains stationary for months with a yellowish discharge, not painful, and tending to spontaneous cure without scarring unless ulcerated from irritation or defective health, should afford sufficiently characteristic features to distinguish framboesia or yaws from other diseases. The principal affection with which it may be confounded is syphilis. From almost the earliest times in which we have any written account of yaws until the present day, the disease has been confounded with syphilis.

Most of the older authorities describe it as the venereal disease; and a few medical men of the present time still believe in its syphilitic nature: but the majority of those observers who have had opportunities of observing both diseases are of opinion that frambœsia is a peculiar disease. The identity of syphilis and frambœsia has recently been supported by Mr. Hutchinson, in his preface to Dr. Numa Rat's essay on the disease, in which it must be admitted the accounts given of so-called yaws are indistinguishable from syphilis, and largely support Mr. Hutchinson's opinion that if "yaws be not syphilis, it is clear that it offers a very exact parallel to it." If yaws really presents the train of symptoms described in some of the cases quoted by Dr. Numa Rat, and upon which Mr. Hutchinson's opinions have been based, the disease is undoubtedly syphilis. From a mere description alone it is difficult for the reader to determine whether in some of Dr. Rat's cases syphilis or tuberculosis were responsible for the symptoms described; on the other hand, from my own personal knowledge of the disease, I discover no warrant for ascribing them to yaws [*vide* p. 253, note].

The present position of the controversy upon the specific nature of frambœsia is mainly one of diagnosis. While Dr. Numa Rat recognises in yaws a peculiar disease, unconnected with syphilis, he appears, in certain cases quoted in his essay, to have mistaken syphilitic and other complications for attributes of yaws, and has classed them in the tertiary stage of that disease. Mr. Hutchinson, on the other hand, accepting Dr. Rat's descriptions of these complications as symptoms of yaws, rightly identifies them with syphilis; thus he is disposed to explain frambœsia proper as syphilis modified by the long operation of the peculiarities of race and climate. These authors may be said, therefore, to be both right and both wrong. My own view of the matter is in accord not only with that of the majority of observers who have studied frambœsia in its native haunts, but also with the opinion expressed by Dr. Alford Nicholls, whose extensive experience and inquiries into this subject have been formulated in a recent report to the Colonial Office. In discussing this matter Nicholls thus writes: "An important point in regard to the question as to whether yaws and syphilis are distinct diseases, is the fact that the granulomata, which could only be secondary or tertiary symptoms of syphilis if they were part of that disease, are essentially the primary manifestations of yaws, and more often than not the only manifestations of that disease. Besides which yaws, which is propagated solely by contagion, attacks young children most frequently; and, even in adults, lesions seldom occur on the genital organs. There is no variation in yaws, no imitation of every other form of skin disease as in syphilis. The typical yaws granuloma is the same in the child as in the adult, in the neglected disease as in the case under proper medical care. It is the same when it first appears as when it comes on in successive crops with long intervals of complete quiescence between."

The localisation of the symptoms to the skin and mucous membranes, when frambœsia is not injudiciously treated, and the fact that the eruption is totally unlike any syphilide (except in the resemblance of the crusts to those of rupia), should readily distinguish it from syphilis. Moreover, rupia begins with a bulla, frambœsia with a solid tubercle. Syphilis never itches, yaws nearly always does. Syphilis is hereditary and known to affect the fœtus in utero, yaws is probably not hereditary and never affects the unborn child. Syphilis is found in all climates, frambœsia is practically confined to the tropics. Syphilis is unaffected by concurrent exanthems, the eruption of yaws is retarded. The differences between yaws and oriental sore are given under the latter disease (*vide* p. 489).

Etiology.—Frambœsia is, as I have said, essentially a disease of the tropics; though possibly the "morula" or button-scurvy of Ireland (now extinct, but described by Wallace, Corrigan, and other writers, from 1823 to 1851, as a contagious disease prevalent in the south and interior of that island) was closely allied to if not identical with it. Neither sex nor age is exempt from yaws, but it is most common in children from one to fifteen years of age. Race has a disposing influence, as negroes are peculiarly liable to it; mulattoes, creoles and pure whites are less susceptible. There is much reason to think that the comparative immunity of the latter is due to the fact that they are less often exposed to contagion. There is little or no evidence to show that either any particular form of *diet* or *heredity* has any special effect on the causation of the disease. What part heredity plays in the extension of frambœsia is difficult to appraise, but it is beyond dispute that children are never born suffering from yaws. It is common enough in young children, but only when there have been opportunities for contact. For some statistical facts on this point Dr. Rat's work should be consulted.

The negroes of the West Indies universally believe that one attack protects against another, and no doubt, as a rule, frambœsia is not contracted twice; but cases are not rare where a second infection has followed a first attack. This, however, is not opposed to our experience in other specific diseases, such as scarlet fever and small-pox. Macgregor says that, in Fiji, the idea prevails that unless a child suffer from *coko* he will not grow up to be a healthy adult; to attain this end, children are either inoculated with the disease or sent to live in the same hut with persons already suffering from it.

Considerable importance has been attached in the past to insanitary conditions of life among negroes and other native populations; but these have only an indirect influence, certainly aggravating the type of the disease, but not producing it. On the other hand, one special fact of prevalence is noticeable, namely, that the local distribution of the disease, in parts where it prevails, coincides with deficient water-supply and the use of artificial tanks for the storage of water. This is probably no mere coincidence, and may point to the water as being in fault and probably the vehicle of the disease.

That frambœsia is contagious is undoubted. Every one who has had any experience of the disease in its endemic centres knows that the affection spreads by contact, and that it is rare to meet with a case where a pre-existent case could not be traced in the immediate surroundings of the patient. It is inoculable through an abrasion or sore, but not through the unbroken cuticle. Ulcers on the foot or leg afford common points of entrance for the virus in negroes. It attacks only those living in contact with the diseased. The uncleanly are more liable to attack than the cleanly; but healthy and cleanly alike take the disease if they are brought into direct contact with the infected. Thus it may be transmitted by sexual intercourse, or from a child to its suckling mother, and conversely. The common house-fly is believed frequently to be the vehicle of contagion; similarly, transmission of the disease may follow wearing the clothes or sleeping on the mat of an affected person. The disease does not seem to be often contracted otherwise than by positive contact of the healthy with the diseased; and aerial infection is practically non-existent. This latter fact is shown by the experiences of those attending the sick in the yaws hospitals, where, so long as the nurses are cleanly and are careful not to abrade the skin, they do not contract the affection. Keelan's experiences in Dominica suggest that vaccination mitigates or prevents frambœsia. He found that of the greater number of cases of the disease which came under his notice, very few were vaccinated; and that the few who had been vaccinated were attacked mildly. This apparently favourable connection between frambœsia and vaccination has not been corroborated by other physicians.

Of interest in relation to the etiology of this disease is the fact that fowls suffer from tubercles, on the head and parts not well protected by feathers, which closely resemble those seen in man afflicted with frambœsia. Hitherto, in spite of several attempts to transmit the human disease to fowls and animals, no trustworthy evidence has been brought forward to show that this affection of fowls is either inoculable, or that it is identical with yaws in man.

Pathology. — Frambœsia tubercles present no very characteristic histological features. When examined they appear to be composed essentially of granulation tissue, which represents a dermatitis confined mainly to the papillary layer, extending more or less into the corium and involving the skin glands and hair follicles. The epidermis is usually detached, and the rete infiltrated with leucocytes. The exciting cause of these inflammatory changes is undoubtedly a specific infective virus. Pierez describes a micrococcus, which he obtained from tubercles of frambœsia, which he is disposed to regard as the exciting organism; but he has not shown that a disease, identical with frambœsia, results in an animal inoculated with a pure culture of this micrococcus. Apparently the same micrococcus has been constantly found by Nicholls in the secretions from the granulomas characteristic of yaws, and also in abundance in the tissues of persons suffering from the disease; no other pathogenetic microbe being found in association with it. In no instance was this micro-organism discovered in the blood, although it has been successfully cultivated in serum. Pure cultures of this micrococcus of yaws show that its microscopical characters are constant, and that its macroscopical reactions differ from those of all other micrococci. The lower animals are probably immune, inoculations giving negative results, as does likewise inoculation with secretions from the granuloma. In the absence of the conclusive proofs of the pathogenesis of this microbe—namely, the production of the disease in healthy animals, and the after-discovery of the micro-organism in the fluids or tissues—it cannot be positively declared that the microbe is the contagium of the disease, however probable this may be. It seems to invade the system through the lymphatics. It is important, in connection with the mode of propagation of this malady, to observe that the micro-organism has been found by Nicholls in the dust on the floor of rooms in which yaws patients have been living; and that, as a matter of experiment, it is capable of retaining its powers of growth and multiplication for a considerable time. The clinging of the contagion to certain huts and localities, and the occurrence of a sudden outbreak of the disease when the heavy rains of a tropical climate moisten the earthen floors, seem thus to be explained.

Treatment.—Recognising that frambœsia is a highly contagious disease, the first duty is to secure adequate isolation of the sick person. In Dominica, Grenada, and St. Lucia this first principle of prophylaxis is so well realised that infected persons are compelled to go into a yaw hospital under penalty of imprisonment. Compulsory segregation of the infected sick by themselves is, however, insufficient; no system of dealing with the disease can be considered efficient that does not further provide for (*a*) the isolation, as far as possible, of infected houses; (*b*) the thorough disinfection afterwards of these houses, and the destruction or disinfection of the clothes and bedding used by the sick; (*c*) the demolition of the wretched hovels, so common in endemic centres of this affection, which, by reason of the clinging of contagion to them, are so constant a danger to the public health; (*d*) a rigid enforcement of ordinary sanitary precautions; (*e*) the compulsory notification of all cases of yaws to the local sanitary authority.

The first essential in the actual treatment of the attack is the cleansing of the patient by means of warm baths and soap. Special care must be taken to avoid chills; as exposure to cold often causes a disappearance of the eruption, accompanied by much constitutional disturbance. The food must be nourishing, consisting of fresh meat, fish, rice, yams and diluent drinks, combined with medicinal tonics. Locally, disinfectant lotions of boric or carbolic acids, or of corrosive sublimate, are of the first importance. Sulphate of copper is efficacious as a topical application; so likewise are iodoform and weak nitrate of mercury ointment. The use of mercury in this disease needs the utmost care and supervision, as its abuse has been largely responsible in the past for the severity and fatality of many cases: it cannot be regarded as a specific remedy for the disease, as it is for syphilis, but, given in minute doses for a short time, mercury seems to act as a beneficial alterative. Of other internal remedies iodide of potassium with arsenic is very valuable, while in some cases iron and sulpho-carbolate of calcium are of the greatest benefit. Arsenic is very successful in the cases in which the eruption is badly developed or scaly, as in the *pian dartre* variety. When the feet and hands are affected, prolonged soaking in hot water is often required in order to soften and remove the thick epidermis; the exposed yaw growth can then be successfully treated on the lines indicated above.

During convalescence iron and arsenic are both to be administered over long periods; while in all stages of the affection perfect cleanliness and the best hygienic conditions are needed, both for the sake of the sick and of those brought into contact with them.

R. H. Firth.

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R. H. F.

INFECTIVE DISEASES COMMUNICABLE FROM ANIMALS TO MAN

(*a*) OF CERTAIN BACTERIOLOGY

37. GLANDERS 38. ANTHRAX

GLANDERS (FARCY)

Synonyms.—Gk. Μᾶλις, or Μῆλις; Lat. *Malleus, Equinia;*
Fr. *La morve, Le farcin;* Germ. *Rotzkrankheit.*

About the end of the fourteenth century (1370-90), Vegetius gave the first systematic description of a malady which he named "Farcinium"—the farcy of more modern writers. The glanders or malleus of to-day has long been recognised as a distinct disease; though in the earlier stages of its evolution it resembles in some respects simple catarrhal inflammation of the nose, and afterwards either pyæmia or tuberculosis; so that while on the one hand it was often mistaken for these maladies, these again were often diagnosed as glanders. Thus the whole subject lay long in confusion.

Glanders, which as a primary lesion has been most fully described in the horse, derives its name from the presence, in advanced cases, of enlarged glands in the submaxillary and parotid regions; the enlargement of these glands being apparently due to the action of a specific irritant, which makes its way inwards from the surface of the mucous membrane of the nasal respiratory passages, initiating well-marked and characteristic lesions in the mucous membrane and in the submucous tissues of these passages.

Symptoms.—In many cases of glanders there are absolutely no symptoms on which a trustworthy diagnosis may be founded; and it is only since the use of mallein has become properly understood that any accurate estimate of the number of glandered horses in the stables of our large towns has become possible. The earlier descriptions of the symptoms have almost invariably been taken from ordinary cases of advanced glanders, and are now therefore of comparatively little value except from an historical point of view. The earliest symptom in the horse is usually an unaccountable *loss of condition.* The patient appears to be under exactly the same management as regards food and appetite, general hygiene, exercise and work; but he falls off in general condition. This is often accompanied by more or less polyuria, and is generally followed by swelling of one or other of the limbs, usually of the hind leg, in which there is found a kind of inflammation of the lymphatic system—*glanderous lymphangitis;* "farcy buds" and "swollen leg" often being marked features of the disease at this stage.

Following or accompanying these symptoms, *submaxillary enlargement and induration* afford still more positive evidence of the presence of the glanderous condition; and a short dry cough, indicating the presence of some lesion in the lungs, is often met with, sometimes before any other symptom has had time to manifest itself. The frequent occurrence of this cough is readily understood when it is borne in mind that in both farcy and glanders the lungs are so frequently involved that it is held that in every case a lung lesion may be found if a careful enough search be made. It is sometimes stated that a thin, watery discharge, which gradually becomes thick, viscid and glue-like, sero-purulent, bloody, and often extremely offensive, is pathognomonic of this disease, and that it should always be looked for. When present, such discharge may help us to form a correct diagnosis; but it has been abundantly proved that no great reliance can be placed on this featûre, as it is only found in those cases in which nasal ulceration has made its appearance,—an ulceration which occurs in a very small proportion of the cases that come up for examination, and in these in the later stages of the disease only. On examining the mucous membrane of the nose in an advanced case of glanders, especially that on the *septum nasi*, it is found greatly congested in certain areas; in some cases, however, it presents a dull leaden colour. On the septum nasi, which should always be examined, small shotty nodules, usually surrounded by a congested zone, may be seen in the early stages of the disease; after a time these nodules become pale in the centre, soften and ulcerate, the softened central portion escaping and leaving a small, deep, circular ulcer with a sharply-defined edge, as though the ulcer had been punched out. As these ulcers increase in number they gradually run together, and form serpiginous ulcers, which once recognised cannot easily be mistaken for anything else. The whole of the ulceration on the septum is not, however, of this character. In some specimens preserved at the Royal Veterinary College in Camden Town, there is, as pointed out by Prof. M'Fadyean, a kind of superficial erosion; beneath these eroded surfaces there appears to be very little infiltration, and it may be that this superficial ulceration or erosion is due to the action of the irritant or caustic discharge from some of the punched-out ulcers on the surface of the mucous membrane over which it flows. The two conditions are perfectly distinct, though the second form is not usually noted. With the ulceration there is often swelling of the nasal mucous membrane, with consequent obstruction of the respiratory passages and a peculiar "choking" breathing. At this stage marked submaxillary lymphadenitis is often present. The glands, usually swollen and indurated, seem little disposed to undergo suppurative changes. The disease may spread to the frontal sinuses; the skin on the forehead becomes thickened and tender; the subcutaneous lymphatics in the face and neck usually enlarge, and when opened are frequently found to contain soft, greasy, pyoid material. The swollen lymphatics are the so-called *farcy-pipes*. Along their course nodular dilatations may usually be seen, which are said to occupy the sites behind the valves of the lymphatics. In "*button-farcy*," moreover, small tubercular nodules are met with in the skin. The limbs (especially the thighs of both hind limbs), usually affected at an early stage, are stiff, hot, and tender; abscesses form, sometimes subcutaneously, at other times apparently in the substance of the muscles. The matter from a newly-opened farcy bud has, as a rule, very distinctive characters; it is glairy or oily, and contains but a small number of leucocytes, so that it is usually distinguishable from staphylococcus pus, and strangles pus. A most important fact is that glanders bacilli are seldom, if ever, very abundant in farcy pus; but, on the other hand, other organisms, such as staphylococci and streptococci, are seldom if ever present. It follows, therefore—and this is the result of general experience—that if, on microscopical examination, no bacteria can be found in the matter from a comparatively superficial lesion, such lesion is glanderous in its nature; and cultivation or inoculation experiments usually demonstrate the presence of the bacillus mallei in such matter, even when present in very small numbers. The appetite, at first good, gradually becomes impaired; the animal loses its strength and flesh; the cough gets worse; the abdomen is retracted; the coat, staring at first, gradually falls off, and the animal dies of exhaustion.

Pathology.—It is almost invariably found that the lungs are involved. The best description of the typical lesions of glanders is that given by M'Fadyean, on whose description of the pulmonary lesion the following account is based: [1]—On passing the hand over the surface of a lung affected with glanders, firm, hard nodules may be felt not only immediately under the pleura, but also, on deeper palpation, at some distance from the surface. On section, pearly gray nodules, some with a peculiar yellowish-white centre and surrounded by a dark, hæmorrhage-like zone, may be seen; these vary in size from points just visible to the naked eye to nodules the size of a pea, a hazel nut, or even a walnut—the pea-sized nodules being the most abundant. I have seen a glandered lung in which only a couple of these nodules could be made out; whilst in others the number has varied from a dozen up to several hundreds in each lung. These nodules, however, can never be spoken of as innumerable; so that in this respect they differ from true pulmonary tubercles, which, in the horse, if not innumerable, can be counted by thousands. Sometimes dark hæmorrhagic areas may be noticed in the lung, in which, scattered at intervals, are gray nodules similar to those above described. Within a grayish capsule is a white centre which may be somewhat softened; though it seldom undergoes purulent degeneration. When the centre is firm it may often be "easily shelled out with the point of a scalpel from the grayish peripheral portion"; in some cases this central portion undergoes calcareous degeneration. On examining the hæmorrhage-like areas under the microscope, it is found that the central zone consists of lung tissue densely packed with polynuclear leucocytes or pus corpuscles, which occupy the alveoli and compress the septa; in this region there is little or no proliferation of the epithelial cells lining the alveoli. Immediately around this area is a zone in which may be seen numerous epithelioid cells, each of which contains a single vesicular nucleus, which does not stain nearly so deeply as does the polynuclear form; here also a few giant cells may be found among the epithelioid cells. Except at the margin of this zone, it is difficult to make out the remains of the walls of the air vesicles; but immediately outside this is a third zone in which, owing to thickening of the walls, the air vesicles are considerably smaller than normal. The thickened septa are composed of fibrous tissue with elongated nuclei; whilst the cavity or vesicle contains a lining of more or less cubical epithelial cells, a number of free epithelioid cells, a few leucocytes, and large uninuclear cells containing particles of carbon. Here too may be seen a few strands of coagulated fibrinous lymph. Surrounding this area is a zone in which the changes are indistinguishable from those found in croupous pneumonia; the interalveolar capillaries are distended with blood, and the alveoli contain delicate coagula in which leucocytes, detached epithelial cells, and a few red blood corpuscles are entangled in a network of coagulable fibrinous lymph. It appears that this pneumonic condition is the first indication to the naked eye of the presence of a glanders nodule; although by careful microscopic examination we learn that the small area of infiltrated leucocytes is the primary focus of change. This small area becomes surrounded by a pneumonic zone, in which thickening of the alveolar walls and packing of the alveoli with various kinds of cells may be observed; the process spreads from the centre outwards, the pneumonic zone indicating the part most recently affected. When the process is more chronic this so-called hæmorrhagic appearance is absent, and the centre of the nodule, as it softens, is found to be composed of leucocytes and granular detritus; outside this is a zone in which large epithelioid cells are abundant, and amongst them a few giant cells which are indistinguishable from those met with in a tubercular nodule. The pearl-gray capsule, as in tubercle, is made up of connective tissue in various stages of development, whilst immediately outside this is a zone which consists of cirrhotic lung tissue, in which the walls of the alveoli are enormously thickened; the air vesicles are correspondingly diminished in size, and are lined by distinctly cubical epithelium: this part of the lung tissue closely resembles the white pneumonia described by Virchow in the lungs of syphilitic children, a condition which is also found in other forms of interstitial pneumonia occurring in the adult. As in these conditions, there is in glanders also considerable injection of the vessels in this new tissue; and there may be fibrinous exudation into the air vesicles just beyond the area of the healthy lung. As in tubercle, a central area may shrink and become calcified; and this area, being often surrounded by a distinct fibrous capsule, represents the nearest approach to healing and isolation that ever occurs in the case of a glanders tubercle. M'Fadyean believes that in the horse the tubercles originate in connection with the air vesicles, but whether in consequence of the arrest of glanders bacilli in an alveolar capillary, or of the penetration of the bacilli into a vesicle with the respired air, he does not say; he inclines, however, to the belief that, as the nodules are comparatively few in number, and are often confined to one lung, they are not spread by the blood; moreover, the irregular distribution and the difference of age of the tubercles point rather to a dissemination of the bacilli by the air-passages. If the starting-point of the tubercle be the multiplication of bacilli that have come to rest in the cavity of an air vesicle, infective matter may find its way from this point along the bronchi to other portions of the lung, to form fresh foci of disease. In support of this view we have the fact that the small bronchi often contain numerous leucocytes, some in various stages of degeneration; whilst evidence of proliferation in the perivascular lymphatics is comparatively rare. In certain cases, indeed, the lymphatic system seems to be more directly invaded; but such invasion appears to go on much more slowly and in a much more localised fashion than in the case of tubercle; the lymphatic glands are seldom enlarged, and, in marked contradistinction to the glands in tubercle, they present remarkably few changes of any kind, especially when examined merely with the naked eye. In consequence, however, of such a lymphatic infection large areas of the lung tissue may be more or less consolidated; the interlobular septa are thickened and fibrous-looking, whilst between these there is evidently a pneumonic exudation from which a little clear fluid may escape. This mass of lung tissue is usually moist and of a pinkish colour, and here and there in it small white points may be distinguished. These points, when examined under the microscope, are found to consist of a group of air cells, crowded with leucocytes surrounded by a number of epithelioid cells; whilst the pink, consolidated, moist mass consists simply of lung tissue in a state of croupous pneumonia, in which the lymphatics of the thickened interlobular septa are found to contain an exudation similar to that present in the air vesicles. In certain cases the solidified portion of the lung, usually the lower edge, is more like the white pneumonia of Virchow already mentioned. In this consolidated mass we find a condition of chronic bronchitis and peribronchitis, the whole bronchial wall being apparently replaced by a granulation tissue consisting of round cells and young connective tissue; whilst in the lung about it we have a condition of chronic interstitial pneumonia. This is usually associated with the presence of nodules of glanders in other parts of the lungs. When the nodules are close to the surface of the lung the overlying pleura is always thickened, especially in its deeper layer, where the thickening is often the result of irritation of the lymphatics, resulting in the formation of fibrous connective tissue; it is sometimes associated also with the development of villous fibrous granulations on the pleural surface.

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[1] Through the kindness of Professor M'Fadyean I have been enabled to make an examination of these lesions of the lung, and also of other tissues.

It is evident that glanders must be looked upon as the local and outward manifestation, or as the group of primary phenomena of a peculiar pyæmic condition which may be spoken of as farcy; indeed, one writer (Bendall) says that as the malignant pustule of charbon in man is to the constitutional blood-poisoning of anthrax, so the local glanderous affection of the nose is to the general pyæmia of farcy.

Farcy is seldom a primary disease in the horse, but it appears to be the usual form of the disease in the human subject, in whom it assumes a form similar to glanders experimentally produced. In experimental glanders the malady usually appears as an acute or generalised pyæmic state, and the discharge from the nose and other nasal symptoms make their appearance in the later and more chronic stages of the disease. These later stages are usually characterised by the presence of minute nodular new growths very similar in structure to those described in the lung of the horse; and are made up of small round cells, which are very apt to undergo disintegration, especially in the centre, and thus to give rise to minute abscesses and ulcers. These nodules are found most frequently in the skin and subcutaneous tissue, in the mucous membranes of the organs of respiration, and, though less frequently, in the internal organs. In acute cases the ulcers, which as a rule are exceedingly foul, seldom heal; but in cases of chronic glanders, healing, partial or complete, often occurs. Farcy in man has been well described as taking the form of an acute or, more rarely, a chronic specific pyæmia, characterised by eruptions on the skin, on the nasal mucous membrane, or on both, frequently accompanied by the formation of intramuscular abscesses. In the human subject the glands are rarely specially affected; there is usually inflammatory œdema and swelling of the limbs, with intramuscular abscesses sometimes of enormous size. Infection usually takes place by inoculation of a cut or abraded surface with the discharge from a glandered animal; or a similar inoculation may occur during an operation or a dissection of such an animal. Farcy is found, therefore, in stablemen, knackers, and others who are brought into direct contact with glandered horses. Babes performed a series of experiments to demonstrate that glanders bacilli can set up infection when rubbed with lanolin and lard into the healthy skin of guinea-pigs. Nocard arrived at a similar conclusion, and found that the bacilli were readily absorbed, especially from the mucous membranes of the eyelids, nostrils, and larynx. It is supposed that the bacilli make their way into the various follicles, especially into those of the hairs, that they multiply there, and gradually make their way thence through the epithelium into the deeper tissues, whence they pass by the lymphatics and even by the blood-vessels to various parts of the body.

The period of incubation after inoculation is very short. The first signs and symptoms of the onset of the disease are local swelling, pains in the joints and limbs, and then marked inflammation of the lymphatics accompanied by high fever. All these symptoms appear within twenty-four hours. Suppuration comes on within forty-eight hours, and the abscess rapidly points. At this period the symptoms are those of pyæmia. Should the patient survive, the wound may heal. This is more likely to occur when the disease is contracted through an old wound, or when there is no apparent wound. In such a case the period of incubation may be prolonged to one or two weeks, or even more. Under these conditions the first symptoms are malaise, headache, nausea and vomiting, pains and tenderness in the epigastrium and hypochondrium, and, less frequently, in the back, joints and limbs. Then come rigors, followed by full pulse, furring of the tongue, great thirst and scanty secretions, accompanied by severe rheumatic pain in the muscles and joints. During this stage the disease may readily be mistaken for an attack of acute rheumatism. Hard tumours in the muscles of the limbs near the joints on both sides of the body may then make their appearance. These soften, point, and burst, leaving huge foul ulcers, and ultimately, sinuses. Abscesses, the only constant pathological feature of the disease, become more numerous, and are usually symmetrically disposed in the limbs. An asthenic febrile condition supervenes, often followed by a "typhoid" state; which indeed may set in early, accompanied by deafness, stupor, delirium, coma, or complete unconsciousness. The disease when met with in this form is frequently diagnosed as chronic pyæmia. These general conditions are, however, usually accompanied by other sets of symptoms, some of which are fairly characteristic; such as painful swelling of the nose, in which dried crusts of mucus mixed with pus and blood may accumulate and give rise to marked obstruction; or serous fluid may be discharged, which later becomes muco-purulent, or streaked with blood, and very offensive. Dyspnœa is a marked symptom. In some cases there is an exceedingly fœtid diarrhœa; in others, as in many other specific infective fevers, the urine may be heavily loaded with albumin. The appearance of early fœtid serous or purulent discharge from the nares with consequent stuffing of the nostrils by inspissated pus and mucus, ecchymosis of the conjunctivæ, and febrile symptoms may, when acute, be called pathognomonic signs of farcy.

Farcy may further be distinguished from ordinary pyæmia by the presence of various skin eruptions. The more common of these are small circumscribed erysipelatous patches, which very closely simulate erythema nodosum. These patches often become the seat of pustules or of phlyctenæ, whilst in some cases gangrene of the skin supervenes. Bullæ of various sizes, containing a sero-purulent fluid, are also often met with: when they burst a raw surface is left, or if they dry up a hard crust, often mixed with blood, remains to mark the seat of the bulla. A pustular rash somewhat like that of small-pox, but without umbilicated pustules, is also often met with. The pustules are somewhat irregular in shape and size; they are placed on an inflamed base, and they may be surrounded by a white wheal-like ring. In some cases marked œdematous swelling, similar to that observed around the abscess in other parts of the body, surrounds the furuncles, especially those situated on the face. This pustular rash is of very grave significance, as when it once makes its appearance recovery seldom if ever takes place. The muscular abscesses, which, as already mentioned, are often multiple and symmetrical in the limbs, and which appear to be the result of infarctions, often point beneath bullous pustular patches, or are covered by intensely inflamed skin. These intramuscular abscesses are often hæmorrhagic, the pus is dirty and unhealthy-looking, and contains sloughs and débris, blood and pus cells and, according to Bendall, a considerable quantity of free oil. They form rapidly, usually in the neighbourhood of joints; the tissues around them are soft, sodden, and break down readily, no pyogenetic membrane being found; so that the pus often infiltrates the intermuscular tissues, and sometimes makes its way into joints. Pus is often found also in the internal organs; in the kidney, between the stomach and spleen, in the posterior lobe of the brain, in the shafts of the bones, and separating cartilage from bone. In acute cases small abscesses, similar to those in the lung, are also found in the skin and mucous membrane. In the human subject a metastatic lobular pneumonia, almost identical with that met with in the horse, is often observed: it is, however, more acute, there is often intense congestion around the pneumonic area, and the centre of this area undergoes marked softening. In or around this pneumonic area the arterioles and capillaries may contain fat or oily emboli (Bendall); a condition supposed to be due to the absorption of fat from the rapidly degenerating or fatty necrotic tissue of the nodules. As might be expected, extravasations of blood from the obstructed capillaries often take place into the surrounding tissues. In chronic farcy these lung complications are comparatively rare. In acute glanders in man abscesses in the bone marrow have been described. Bronchitis is comparatively common in acute cases, especially when the lung is affected: there is marked catarrh of the epithelial cells covering the mucous membrane, whilst the epithelial cells of the muciparous glands may disappear altogether. The pustules and nodules, both in the nasal mucous membrane and in the skin, appear to have a similar structure and course to those nodules met with in the internal organs; these have been summed up thus: (i.) An accumulation of cells, which (ii.) rapidly undergo degenerative changes; (iii.) congestion of the surrounding vessels; (iv.) ulceration of the degenerated tissue, which is usually preceded by (v.) proliferation of the epithelial covering of the papillæ. The ulcers, as already mentioned, usually occur in groups and, gradually coalescing, form a serpiginous ulcer often of considerable size. The extravasations of blood, so frequently met with in this condition, come from the distended vessels. Similar pustules and ulcerations, with exactly the same structure, have been described on the hard palate and in the larynx. Lymphangitis when present is usually the result of direct infection through a wound. Acute farcy is an exceedingly fatal disease; only some 4 to 8 per cent of the patients recover. Death takes place in from one to three weeks. In chronic farcy the fatality is not nearly so great. According to some observers over 60 per cent recover; the disease running its course in about four months.

Babes describes a condition in man, which corresponds to the masked or latent glanders in the horse, in which encapsuled nodules are found.

especially in the lungs; such cases can only be diagnosed during life by the use of mallein. In one case, in a groom who died from chronic nephritis, nodules were found in various parts of the body; from these nodules cultures of the bacillus mallei were obtained. Another series of cases is mentioned, usually in coachmen, grooms or men whose work is amongst horses, in whom death was apparently due to intercurrent diseases; in them, after death, have been found nodules identical with those found in latent glanders of the equine species: these cases are supposed to be cured or in a fair way to recover. The lesion invariably consists of a nodule or mass of hard sclerotic tissue with a calcified centre; these nodules are found studding the lungs, and are usually accompanied by pleural adhesions of old standing. They may also be found in the mediastinal and bronchial glands, and in the spleen and liver. The lesions in one of these cases of mixed glanders took the form of chronic ulceration of the leg, which first healed, then broke out again, and after a time was followed by high fever, local gangrene, and the formation of an abscess in the cellular tissues of the leg. In this case the organisms present were found to be staphylococcus pyogenes aureus and the bacillus mallei; from which Babes concludes that the attenuated glanders bacilli may give rise to the formation of chronic nodules, which do not become acute until certain pus organisms gain access to them. These mixed infections, however, are of comparatively rare occurrence, and few observers have been able to corroborate Babes on this point.

Bacteriology.—If the pus or broken-down tissue from an actively growing glanders nodule be mixed with a little sterile saline solution, and a small portion of this be allowed to trickle over the cut surface of a sterile potato, and then kept at the temperature of the body, bright yellow or honey-coloured colonies soon make their appearance, and grow so luxuriantly that in eight or ten days the colonies of other organisms, if any, are overgrown; the growth going on more rapidly as the colonies become larger and run together. In these later stages the shining or glistening surface assumes a peculiar fawn-brown, and ultimately may assume a chocolate or *café-au-lait* colour. The *bacillus* when examined under the microscope is about as long as the tubercle bacillus, but considerably thicker; no spores are formed in its substance, but sometimes its protoplasm is fragmented. It is said to be non-motile; but some observers maintain that, under certain conditions, these bacilli have the power of motion. It will grow in or on almost any of the ordinary cultivation media, especially when they are made slightly acid and are kept at the temperature of the body. In gelatine it forms a whitish growth made up of chains and threads coiled irregularly and penetrating the gelatine in various directions. On agar-agar it has a grayish-yellow tinge. On glycerine agar-agar it grows luxuriantly (even at the temperature of the room), as a broad, white, transparent line, which follows the track of the needle. On a *purée* of potato, or in potato gelatine, it forms prominent translucent plates, with a grayish periphery and a shining, fawn-coloured central part.

It is most difficult to stain the organism differentially when in the tissues; as, although it takes the aniline dyes very greedily, it gives them up with almost equal readiness. Noniewicz's method (10) for staining the bacillus is to stain for two to five minutes in Löffler's methylene blue (concentrated alcoholic solution of methylene blue 30 c.c.; caustic potash 0·01 per cent solution 100 c.c.), to wash in distilled water, and then decolorise for from one to five seconds, according to the thickness of the section, in a mixture of 75 parts of a 0·5 per cent solution of acetic acid and 25 parts of 0·5 per cent watery solution of tropæolin; to wash again in distilled water, and, after spreading the section on a slide, to dry it first with blotting-paper, and then in the air or over a spirit flame. Clear by dropping xylol upon it (oil of cloves, origanum, and aniline oils must be avoided), and mount in Canada balsam. The bacilli are stained dark blue or nearly black, and the tissue light blue.

As it is sometimes exceedingly difficult to obtain cultures from nodules of glanders it has been found advisable, for diagnostic purposes, to inoculate a guinea-pig or a field mouse with portions of the suspected material. In a guinea-pig, after subcutaneous inoculation—say in the back—with the glanderous material from which the diagnosis is to be made, tumefaction appears at the seat of inoculation, the skin ulcerates, and a mass of soft, almost purulent material is discharged, a chronic ulcer being left, with irregular indurated margins, from which issues a sero-purulent discharge. In some cases this ulcer may heal; the lymphatic glands in the neighbourhood, however, become enlarged, and may also ulcerate; and at the end of four or five weeks the animal becomes generally infected. In the male the testicles are swollen; and later an acute inflammation causes considerable enlargement of the joints. Field mice similarly inoculated die in three or four days. Intraperitoneal injection of an emulsion of the suspected material, or of a discharge from an ulcerated mucous membrane or gland, sets up a much earlier inflammation of the testicles: this often occurs as early as the third or fourth day, and in the fluid between the two layers of the tunica vaginalis testis glanders bacilli may be easily demonstrated, either by microscopic examination or by the culture test. Pure cultures of the bacillus mallei injected into horses, rabbits, and the animals already mentioned, produce typical glanders of the constitutional type. Ordinary house mice are more refractory, but they also may be infected by very virulent bacilli. Lions and tigers are said to contract the disease. In these experimental cases there is inflammation of the lymphatics and orchitis; the nasal mucous membrane is not affected until the later stages of the disease. One case of direct infection in the human subject was traced to the use of an imperfectly sterilised hypodermic syringe with which cultures of the glanders bacillus had been injected. The specific bacillus may rarely be associated with streptococci and staphylococcus pyogenes aureus; and it is probably this latter organism that gives rise to the peculiar phlegmonous lesions which are sometimes met with during the course of an attack of glanders.

The glanders bacilli if kept moist may remain alive for a month; but Bonome says that when dried they die within about ten days. In distilled water they succumb in about five days. They are killed at a temperature of 55° C. They may remain alive when grown on culture media for about a month.

The disease is spread principally by the discharges, and by such secretions or excretions as urine and milk; though diseased organs and tissue may also serve as foci from which the disease may spread. Sherrington and Bonome both find that this bacillus can pass through the kidneys, even when there is no lesion to be made out, either with the naked eye or under the microscope. Bonome also maintains that the glanders bacillus passes from the parent to the fœtus, not only at those points at which placental hæmorrhages occur, but in some cases where the structure of the placenta appears to be perfectly normal. When the bacillus mallei is found in the circulating blood the disease runs an exceedingly rapid course, and the patient succumbs with most acute symptoms.

It has been found that the glanders bacillus when cultivated as a saprophyte loses its virulence very rapidly; and, under certain conditions, it so far loses its activity as to set up an exceedingly modified form of the disease in the horse: for, although it is stated that an unoccupied stable has remained infected for a period of a year and a half, most observers remind us that if the organism exist outside the tissues for any such period it becomes greatly attenuated. Although this organism grows best in the presence of oxygen, it is capable of growing anaerobically; indeed when so grown it appears to have a greater power of forming toxins than when it has access to a free supply of oxygen. It has been stated that the virus may be attenuated by passing it through a series of cats, under which conditions it ultimately becomes less virulent for the horse; thus a horse, inoculated with virus so attenuated, passes through a modified attack of the disease, and is then proof against attacks of more virulent cultures of the organism. This observation requires corroboration.

Mallein.—Babes, Kalning, and Hellmann prepared from the bacillus mallei a substance similar to that prepared by Koch from the bacillus tuberculosis. An active toxin forming glanders bacillus (which may be obtained by smearing the pus from a freshly-opened farcy lesion in a horse over the cut surface of a sterilised potato, the discrete colonies being selected as seed material) is cultivated in peptonised bouillon to which a small proportion of glycerine has been added. The culture is incubated at a temperature of 37° C. for a month or six weeks; it is then tested in order to see that the growth is pure—that is, consists of the bacillus mallei only—by inoculating potatoes; after this testing it is placed in the autoclave and heated to 120° C. for twenty minutes or half an hour on each of three successive days in order that all the bacilli may be destroyed. To prevent putrefaction, carbolic acid in the proportion of 0·5 per cent is added, after which the fluid is filtered through a porcelain filter in order to remove the bodies of the bacilli. This fluid contains the active toxic material, secreted by the glanders bacillus, in such quantities that when injected in doses of 1 c.c. it gives rise to a very definite reaction in an average-sized glandered horse; whilst in horses unaffected with glanders no reaction is provoked by a dose of even 6 c.c. As there is some misconception as to the nature of this reaction, it may be stated generally that unless the temperature rise two to four degrees, and a swelling, of three or four inches in diameter and one to one and a half inch in height, appear and continue to increase for a number of hours, after the sixteenth or eighteenth hour the reaction is not characteristic. It should also be borne in mind, as Nocard points out, that this reaction can only be obtained when the temperature is normal; so that mallein should never be injected for diagnostic purposes when the temperature is raised.

Treatment.—Acute farcy in man is so uniformly fatal that treatment is of little avail; in chronic farcy, however, from which 50 to 60 per cent of the cases recover, numerous methods of treatment have from time to time been adopted: iodide of potassium, aconite, mercury, iron, arsenic, and strychnine have all been used in turn. Bendall considers the best treatment, especially in the earlier stages, to be local destruction of the primary sore, the application of chlorinated or similar lotion to the mucous membrane of the nose, and tonics. He adds, however, "in a future case I should open every abscess as it appeared, and administer benzoate of soda at frequent intervals." Bonome recommends the use of carbolic acid in the same way, and there can be little doubt that some such treatment would probably be useful. Bonome, also following Babes, has used mallein in the treatment of chronic glanders in man. He found that injected in doses of two or three drops it was followed by a rise of temperature, then by swelling of the mucous membrane of the eyes and nose, increased frequency of the pulse, and an increase in the secretion of the urine; the respiration remained normal. After several injections these symptoms became less marked; the local œdematous painful swelling, at first a marked feature, soon disappeared; the temperature gradually became subnormal, and there was great polyuria; but no albumin or sugar appeared in the urine. The continued injection of $\frac{1}{20}$th to $\frac{1}{15}$th c.c. of mallein, at intervals of two or three days, was followed in a couple of months by marked improvement, less swelling, healing of the ulcers, diminution in the amount of nasal discharge, and general improvement of the patient's condition. Glandered horses treated in the same way gradually lose the nasal discharge, and the swelling of the glands disappears, and so also the ulcers of the nasal mucous membrane. Prof. M'Fadyean, who has kept horses under observation over considerable periods, has observed that both the local and temperature reactions gradually become less marked and ultimately disappear. How far these amendments are permanent still remains to be seen.

GERMAN SIMS WOODHEAD.

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G. S. W.

ANTHRAX

Synonyms.—*Splenic fever; Wool-sorters' disease; Malignant pustule; Anthracæmia; Charbon; Mal-de-rate; Milzbrand; Mycosis intestinalis.*

From the year 1881 all deaths from anthrax have appeared in the Registrar-General's Reports under the heading "Splenic Fever." As the spleen has no special connection with this disease in man, and is often not affected, the term appears to be inappropriate.

Short Description.—A specific, highly-contagious, and infectious disease, common to man and most vertebrate animals, due to the presence of the bacillus anthracis in the tissues of its host. At the points of introduction it multiplies rapidly, and is conveyed by the circulating blood to all parts of the body; by its enormous numbers, it blocks the capillaries, causing innumerable hæmorrhages in the organs and tissues, and effusions into the serous cavities and cellular tissue; and by its special toxic products, acting on the sympathetic nerve centres, it produces great depression of all vital functions, which often ends in death within a few days.

History.—Anthrax has been known from early historic times. The descriptions given in Biblical and ancient classical records of devastating plagues among domestic animals correspond very closely with those of some destructive epizootics which spread over the continent of Europe during the Middle Ages, and also with others of more recent times, which, although they did not cover such extensive areas of country, destroyed vast numbers of animals, and are known to have been anthrax.

It was not until near the end of the sixteenth century that this disease was suspected to be communicable to man by contagion from animals. The seventeenth and eighteenth centuries were remarkable for the widespread devastation caused by it throughout Europe; and, although it was well known to veterinarians at that time, it was not until towards the close of the eighteenth century that the disease in man, which had previously been considered as carbuncular, was known to be the same as charbon, which was so prevalent among cattle, and to be communicated from them to man. In his work on *Anthrax in Animals*, published in 1780, Chabert separated many septic and gangrenous diseases of the skin from anthrax, under which term they had previously been included; and he subdivided the various forms of the disease into the three divisions which have been mostly accepted by writers almost to the present time. These were: 1. *Charbonous Fever*; internal charbon, without external manifestations. 2. *Essential Charbon*; with primary external lesions—malignant pustule. 3. *Symptomatic Charbon*; internal charbon with secondary external lesions.[1] From his time little advance was made in our knowledge of this disease—save that its contagiousness in animals was proved experimentally by Barthélemy in 1823—until the classical work by Heusinger appeared in 1850.

The important discovery of the **bacillus anthracis,** which is the immediate cause of the disease, was made in the same year by Rayer and Davaine conjointly. They described these "little filiform bodies, in length double the diameter of a blood corpuscle, and having no spontaneous movements," as occurring in the blood of animals that had died of splenic fever; but they failed to recognise their importance. In the year 1855 Pollender published a statement that he had in 1849 noticed a countless number of fine non-motile straight rods without branches in the blood of cattle that had died of anthrax. He asserted the vegetable nature of these bodies, but gave no explanation of their origin. Brauell in 1857 noticed similar bodies in blood which had been taken a few hours before death from a man suffering from anthrax. With this blood he inoculated horses and sheep, and thus produced in them anthrax, from which they died: he did not, however, ascribe any importance to these bodies as a cause of anthrax. Delafond, in 1860, noticed that this organism, when it developed outside the animal body, assumed the form of long, undulating filaments, as distinguished from the short, straight rods seen when it grew within the living body; he further asserted his belief that they originated from spores. During the following few years Pasteur's brilliant researches into the importance of the influence of microbes in fermentation, putrefaction, and various forms of disease, stimulated others to work in the same direction. In 1863, Davaine (10) resumed the investigations which he had discontinued thirteen years before, respecting the influence of the filamentous bodies which he at that time had noticed in the blood of animals which had died from splenic fever. These researches were carried on for many years, till in 1873 he asserted positively that these rods, which he called *bactéridie du charbon*, were the essential cause of this malignant disease; that they were constant in the blood of animals that died from anthrax, and that such blood when filtered and inoculated in animals had no effect. This was confirmed by Koch (25), who in 1876 worked out the life-history of this bacillus. By developing the method of cultivation on solid media outside the body, he succeeded in cultivating the bacilli, and in proving the formation of spores; he also demonstrated that bacilli might be developed from spores. Finally, from the organism thus cultivated, he produced the disease by inoculation in animals. These results were afterwards confirmed by Pasteur, who, in 1877, demonstrated beyond all doubt that these small rod-like bodies, first recorded by Rayer and Davaine in 1850, were the sole cause of this disease. Special interest is attached to this bacillus, as it was the first discovered of all the micro-organisms which have proved to be the immediate cause of infectious disease in man and animals. It is the largest, the best known, and has been the most studied of all the pathogenetic bacteria; it would be no great exaggeration to say that the study of anthrax has been the groundwork of much of our recent bacteriological knowledge.

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[1] Symptomatic charbon, symptomatic anthrax, black quarter, rauschbrand, is a different disease, which attacks only a few species of animals, and is not communicable to mankind. Primary internal anthrax does not give rise to external lesions. While this article is passing through the press I have also deleted the synonyms "Siberian pest; in India, Loodiana disease; in Africa, horse sickness," which indefinite local names sometimes indicate other diseases closely allied to anthrax. The bacillus in "horse sickness," for example, is now said to be shorter than the B. anthracis, although it has like square or concave ends.

1. *Classification.*—The vegetable nature of these rods was recognised by Pollender, Davaine, and Brauell. By Cohn, 1853, they were considered to be related to the lower algæ. Naegeli, 1857, grouped them with the schizomycetes—fission fungi. Cohn's classification of bacteria, according to their morphological and biological characters, has been generally accepted as a provisional arrangement. As recently modified the divisions are:—First, round or ovoid cells—micrococci. Second, elongated, rod-shaped, or thread-like cells—bacilli. Third, curved rods or filaments — spirilla. Flügge includes all bacteria in two divisions; namely, cells spherical or ovoid, and cells cylindrical.

2. *Physical Characters.*—As seen unstained in the blood of animals shortly after death by anthrax, the bacilli are pellucid, round, elongated, rod-like cells, 5 to 20 mm. in length, but commonly about the length of the diameter of a blood corpuscle, and from 1·25 to 1·5 mm. in breadth. They contain a homogeneous protoplasmic material, enclosed in a fine capsule of denser and more highly refractive substance. The ends of the unstained bacillus are straight and at right angles with the longitudinal axis; but as seen with high magnifying powers, and more distinctly with some stains, they are slightly concave. This is a very important feature, and is said to be characteristic of the anthrax bacillus. The bacilli vary somewhat in length and breadth in different species of animals, at different periods of their growth, according to the medium in which they are grown and the method of their preparation for examination.

3. *Growth and Development.*—The normal growth and development of cells, as of every living thing, depend upon many surrounding conditions, of which temperature, air and nourishment are the most important. If the necessary conditions for growth of these bacilli be not favourable;

if certain factors be either in excess or defect, or others deleterious to their nourishment be present, they lose temporarily, and in some cases permanently, their power of producing spores; they may also develop involution forms, appearing as lumpy, irregular bodies which, after passing once through the mouse or other susceptible animal, regain their normal form. The rods and filaments under all conditions are devoid of spontaneous motion. They cannot grow at a temperature below 16° C. (60° F.) or above 45° C. (113° F.); but they multiply most rapidly between 30° and 40° C. (86° to 104° F.) in a neutral or slightly alkaline medium. Moisture and suitable nourishment are also necessary for their growth; but as regards food they are the least exacting of pathogenetic organisms, for they are able to obtain a sufficient supply from almost any source. The organisms are aerobic; they cannot live without oxygen. In the living body they are parasitic, and can abstract from the blood sufficient oxygen to maintain their propagation by elongation at both ends and transverse fission, but not to enable them to grow into long filaments or form spores. In the dead body they grow to a great length without showing lines of transverse segmentation, and with the formation of a few spores only. Outside the body, when they can obtain a free supply of oxygen, they pass through their complete cycle of life and form spores; thus indicating their saprophytic origin. In a suitable nutrient medium, at a temperature of about 37° C. (98° F.), they increase in length, the contents become slightly opaque and granular, and at regular intervals slight swellings of the rods are noticed; at these points the protoplasm appears to collect, becomes more refractile, and presents a well-defined outline which is its capsule; the rod between these bodies, which are now slightly ovate, bright and highly refractile, becomes contracted and separates, the spores are set free, and the rod perishes. These spores elongate at each end, and in two hours grow into bacilli which pass through similar processes of development and decay. The bacilli are tender organisms which disintegrate at a temperature of 60° C. (140° F.) In unopened putrefying carcases they degenerate and die in about a week; in the earth they retain their form, but generally lose their virulence in six months. The spores, however, are very tenacious of life; in a dried state they will retain their vitality for many years, requiring almost burning heat, boiling water, steam under pressure at 110° C. (230° F.), or strong antiseptics to destroy them.

4. *Cultivation.*—When cultivated on the surface of a solid medium—for example, agar-agar or gelatine—with free access of air, they grow into long threads consisting of short segments slightly attached, separated by transverse lines and sometimes containing spores. These threads become long and undulating, and in twenty-four to forty-eight hours a convoluted tangled mass of growth is developed.

The mode of growth in nutrient gelatine (5 to 8 per cent) by needle-stab is very characteristic. In the track of the needle, after a few days, fine, delicate white rays grow outwards and penetrate the gelatine laterally, looking like thistle-down; while liquefaction of the gelatine takes place slowly from the surface. The gelatine liquefies as a grayish, opaque fluid resting on the surface of the lower still solid part of the gelatine. After ten days the whole of it will be liquefied, and the bacilli fallen to the bottom of the tube as a whitish, flocculent deposit.

5. *Attenuation.*—All living beings may be considerably modified in shape, structure, movements and properties by such external agencies as light, gravitation, temperature, or food. By artificial culture new characters can be acquired, which may be permanent. The *bacillus anthracis* under certain conditions loses its virulence without undergoing any morphological change, and in this form, when inoculated, may confer immunity on susceptible animals without apparently producing other effects. The virulence of these bacilli may be diminished or entirely removed by alteration of any of the various conditions under which they reach their most virulent state. Different degrees of attenuation of virus may thus be obtained, some of which will act slightly and others imperceptibly when inoculated on susceptible animals, but are capable, nevertheless, of conferring immunity against the disease. Cultivation in artificial nutrient media at a temperature of 42° to 49° C. (108° to 120° F.), or at a temperature of 19° to 24° C. (66° to 75° F.) for definite periods of time, according to the degree of heat, will greatly diminish their virulence. Pasteur's protective vaccines are prepared in this way. Pressure equal to three or four atmospheres will lessen their power, and six to eight atmospheres will render them inert. Exposure to sunlight, in proportion to its brilliancy and duration, will first diminish and then destroy their virulence; admixture with many kinds of bacteria and antiseptics produces similar effects. The modified organisms thus produced are not pathogenetic, but confer immunity on susceptible animals for nine to twelve months; morphologically, they are indistinguishable from the most active and virulent forms of the organism, and they will generally regain their virulence when favourable conditions are restored, although the degree of virulence varies in different species of animals.

6. *Staining.*—The method of Gram, with methylene blue and eosine as a contrast stain, is perhaps the best. The protoplasmic contents of the cell readily take up the colour, and if overstaining be avoided the capsule and spores may be distinctly seen. When dried they may be mounted in Canada balsam, and will retain their colour for years. [See vol. i. pp. 506-517.]

ANTHRAX IN ANIMALS

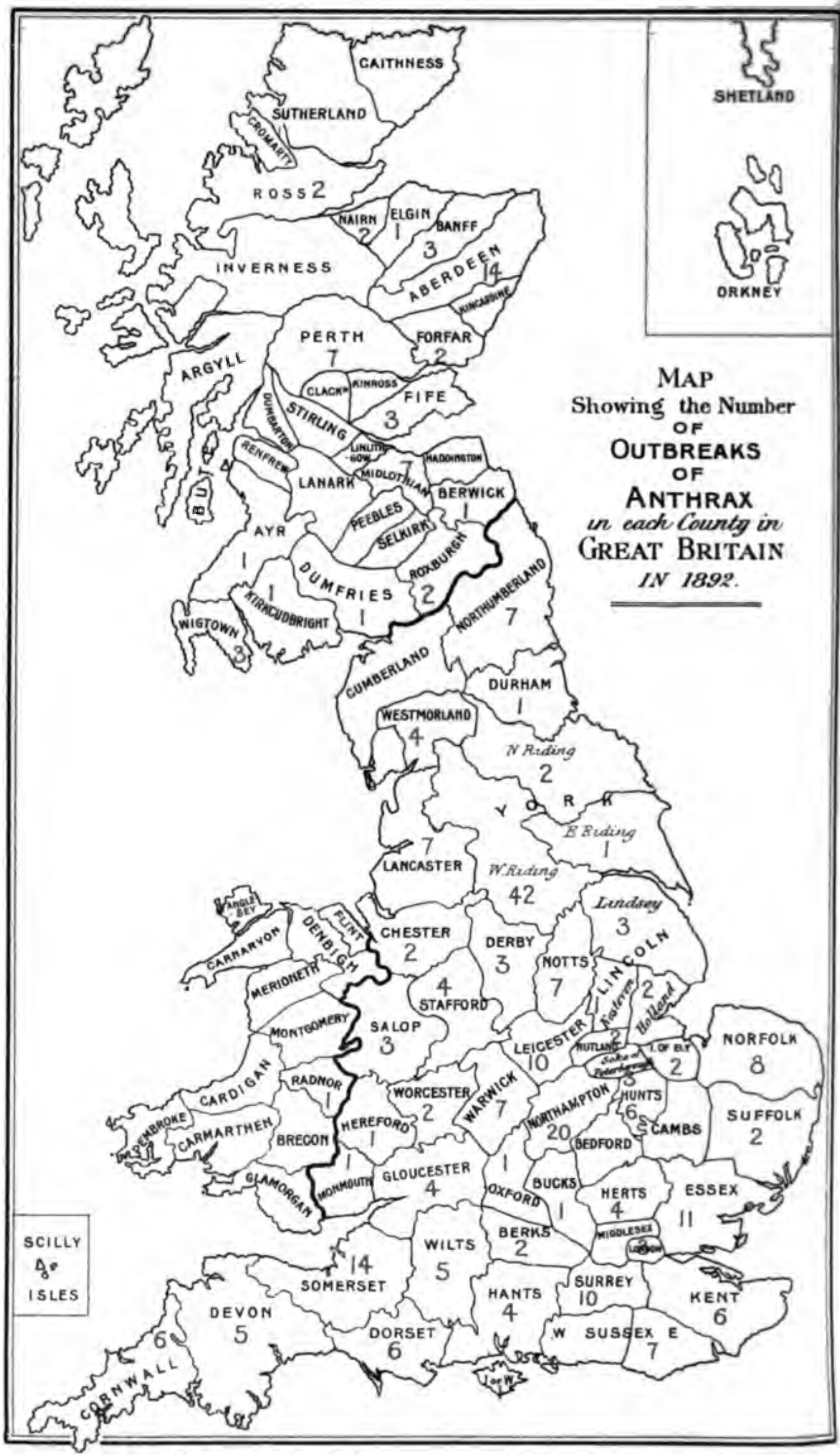
Anthrax is the most widely spread and the most destructive of all contagious diseases which affect animals. It is found in all countries, but is much more prevalent and permanent in some than others, and in some districts of these countries more than in others. It is very prevalent in parts of France, Germany, Italy, Turkey, Persia, India, North and South Africa, and South America; and is least prevalent—although never absent—in Australia, North America, and the British

Isles. During epidemics it may be fatal to from 50 to 70 per cent of the cattle, horses or sheep of a district, and sometimes also it carries off a large number of the population. All classes of vertebrate animals are susceptible to anthrax. The herbivorous mammals, such as cattle, horses, camels, alpacas, sheep, goats and rodents, readily catch the disease. Some of these (as cattle) are very susceptible to intestinal infection, and less so to subcutaneous inoculation; others (as guinea-pigs and white mice) are rarely infected through the alimentary canal, but very readily by experimental inoculation. Some breeds of animals (as Algerian sheep) are but little susceptible, and do not take the disease spontaneously. The omnivorous mammals—such as pigs, dogs, cats and rats—are less susceptible. The carnivorous can only be infected under favourable circumstances as regards age, alimentation, and the virulence or quantity of the material inoculated. Birds, reptiles and fishes are relatively immune; but if the high temperature of birds be diminished, and the low temperature of reptiles and fishes raised by artificial methods, they can be infected like other animals.

Anthrax ordinarily attacks animals by way of the intestines; the food being infected by foreign fodder, litter and manures; or by material from diseased animals exposed to air in pastures and water. The pulmonary form in them is acquired only by experimental inhalation of virulent spores. Subcutaneous inoculation of anthrax virus produces locally a gelatinous swelling of the cellular tissue, but never anything like the malignant pustule of mankind.

The disease does not spread by contact or association; it can only be acquired under ordinary circumstances by the introduction of the infecting organisms into the circulating blood, either through an abrasion or defect of the mucous membrane, or by the spores otherwise finding their way through the epithelium of the alimentary canal, and so causing a general infection. Although "splenic apoplexy" has been known in this country from a remote period as the cause of a large mortality among cattle, it is only since the year 1859 that it has been recognised as anthrax. Since 1886 the disease has been included in the list of maladies which come under the provisions of the Contagious Diseases (Animals) Acts. These are administered by the Board of Agriculture, which prohibits the importation of live animals from infected foreign countries. During the years 1887-95 there were in Great Britain 2741 fresh outbreaks and 6232 animals attacked (exclusive of 461 deer in 1889). The number of outbreaks in 1895 was 434, and of animals attacked 934. It is perhaps too much to hope that we shall soon be able to know as much about outbreaks of this disease when it affects the human species as we do of such attacks when they occur among domestic animals.

Knowing as we do that most of the deaths from this disease in man in this country are caused by infective wools, hairs and hides imported from abroad, the question arises whether our cattle, sheep and other animals are not also often infected by virus derived from these foreign



MAP
Showing the Number
OF
OUTBREAKS
OF
ANTHRAX
in each County in
GREAT BRITAIN
IN 1892.

This map (from the *Annual Report of the Veterinary Department of the Board of Agriculture for the Year 1892*) illustrates the incidence of outbreaks of anthrax in the counties of Great Britain. The distribution of cases varies considerably in different years. In 1890 the total number was 152 against 563 in [illegible]. In all years, however, there is a greater proportionate number of cases in those counties where foreign wools, hairs, hides, and other animal products are manufactured into goods, or otherwise used.

materials. Wools and hairs, used for manufacturing purposes, are imported largely, and are not disinfected but merely washed; the water is discharged into streams or sewers, and the solid refuse from the washing is utilised as manure. It thus readily happens that our domestic animals are poisoned by virus of foreign origin. Notable outbreaks which have occurred in the neighbourhood of Bradford have been traced to this source; and thus we may also account for the excessive number of cases of anthrax which are reported from the West Riding as compared with the East and North Ridings of Yorkshire, and from Leicestershire and Northamptonshire as compared with the surrounding counties. The accompanying map shows that the outbreaks of anthrax are most frequent in those counties of Great Britain where dry foreign wools, hairs, hides and skins are manufactured into goods.

The Governments of Europe, and of many other countries, enforce measures to control the spread of this disease. The most important of these are :—1. The prohibition of the movement of animals from premises on which anthrax has broken out. 2. The cleansing and disinfection of the infected premises. 3. The burial of all carcases—unopened—and everything from them, deep in the ground, and covered with quicklime.

Immunity depends upon certain unknown qualities of the blood or of materials in the blood which, when the virus has been introduced into the body, have the effect of limiting the growth of the bacilli about the point of inoculation; here they become surrounded by leucocytes, and, by a defensive process of phagocytosis, are prevented from gaining access to the general circulation and are destroyed. Of the relative natural immunity of certain kinds of animals I have already spoken. Susceptible animals, however, may be rendered temporarily immune by inoculation with virus which has been attenuated by heat, light, chemicals, the admixture of other bacteria, or, sometimes, by passing it through an animal of a different species. Hueppe and Wood found a species of earth-bacillus, in its morphological development and growth on nutrient media almost identical with the anthrax bacillus, which, when inoculated into susceptible animals, was perfectly harmless, and rendered them immune against anthrax. Wooldridge, by cultivating the anthrax bacillus in an alkaline solution of a proteid body filtered from glands of healthy animals, obtained a fluid free from organisms, a small quantity of which when injected into the rabbit rendered it immune to the action of virulent anthrax material. It has been demonstrated by Hankin and Sidney Martin that an alkaloid and albumoses can be separated from artificial cultures and from the blood and tissues of animals which have died from anthrax; and that these, when given to susceptible animals in adequate but not fatal doses, will produce immunity. [See vol. i. pp. 558-579.]

ANTHRAX IN MAN

This disease is so readily transmitted from the domestic animals to the human species that it must have afflicted mankind from the earliest times. It was known to Arabian, Egyptian, Greek and Roman medical writers, some of whom describe the various stages of the external form of the disease with great accuracy. They all recommended that it should be destroyed by the actual cautery.

Fournier (Dijon) was the first who in 1769 recognised that anthrax—malignant pustule—was not infrequently transmitted to man by the handling of hairs and wools. Montfils in 1776 recorded similar cases. Chabert in 1780 first described other forms of the disease, some with and others without external manifestations. Rayer in 1835 published three cases of malignant pustule, one of which was in a person who was attacked after cleaning Russian horse-hair which for many years had served as stuffing for an easy-chair. Trousseau in 1847 related cases occurring among workers of horse-hair imported from Buenos Ayres. The disease became generally known and understood by medical men and veterinarians in those countries where it was always very prevalent; but it does not appear to have been known as anthrax in England before the publication of Dr. Budd's accurate and complete description of it in 1863. Cases, probably of anthrax, which occurred before this time (as those published by Lawrence in 1847, by Ludlow in 1852, and by Laycock in 1857), were put down to carbuncular or furunculoid disease. Such cases being rare, their correct nature was overlooked, and even recently they have often been unrecognised as anthrax.

The different kinds of anthrax may be classified, according to the part through which the virus gains access to the blood, into—(i.) Cutaneous; (ii.) Intestinal; and (iii.) Pulmonary.

1. CUTANEOUS ANTHRAX—*Malignant Pustule or Vesicle.*—The word pustule is now restricted to those elevations of the tissues which contain pus. The words "Malignant Pustule" in this connection are therefore inappropriate and misleading. The disease is often not malignant, and its pustule never contains pus. Anthrax—a burning coal—is the term usually applied to this form of disease in England and Germany. The general intoxication is known as Anthracæmia. In France the term Charbon (coal) is applied to the local skin affection, and Fièvre Charbonneuse to the general disease. Anthrax in France has the same meaning as carbuncle in England.

Ætiology.—The immediate cause of this form of anthrax is the introduction of the *bacillus anthracis* or its spores into the living tissues and into the blood current through a defect of the epidermis. This may be an abrasion, scratch, cut, prick, bite or sting. It occurs—1. In those who come into contact with living animals suffering from anthrax, as drovers, shepherds, farmers, farriers and veterinary surgeons. 2. In those who touch the carcases of animals that have died from anthrax, as knackers, slaughterers, butchers and others. 3. In those who handle offal, skins, hoofs, horns, hairs, wools or other derivatives from such diseased animals, as tanners, fell-mongers, wool-workers, hair-workers, horn-workers, rag-sorters, plasterers, furriers, felt-makers, brush-makers, mattress-makers, and so forth. 4. In those who have a less direct connection with infective materials—who live, for instance, in the neighbourhood of such manufactories. In countries where the disease is common among animals, women and children, who do not come into direct connection with infective material, are not infrequently attacked with the disease through the medium of persons, animals or insects. 5. It has several times been transmitted from one person to another, with fatal results—as at a post-mortem examination. A wife is also reported to have taken it by touching her cheek with her hands when dressing the sore of her husband. In some undoubted cases the source of the infection cannot be traced. It is probable that persons who eat very little animal food are more susceptible to the disease.

The lesion may appear on any part of the skin. In more than 99 per cent of the cases recorded in this country, it appeared on some exposed part, such as the arm, face, neck or chest. There is generally only one point of inoculation: occasionally two are seen, much more rarely three; the lesions progress simultaneously.

When the disease has been entirely local, it probably does not confer any protection against a future attack; when it has also been general, it affords some degree of protection: cases are recorded, however, of persons, after a few years' interval, having a second and even a third attack.

Malignant anthrax œdema without cutaneous lesion—œdème-malin of Bourgeois—has not been observed in this country; neither has any case been recorded elsewhere in which the anthrax bacillus was proved to be present. It is probable that this term has been applied to those very rare cases which have no characteristic eschar, but which have always some lesion of the skin at the point of inoculation.

Incubation.—The period of incubation varies with the method of inoculation, and the quantity and virulence of the poison. When it is introduced by the bite of a fly, or the sting of an insect, the additional poison immediately arouses a painful itching and rapid inflammation of the skin. Where an inflamed pimple has been scratched, and inoculated at the same time, or shortly afterwards, development is almost equally rapid. When the virus is introduced by a cut or abrasion of healthy skin, there will be some itching on the following day, with swelling and inflammation on the third day. When the infecting material is fresh, and in the bacillary form, incubation will be shorter than when dried spores are the infecting agent. When the period of incubation appears to be longer than two or three days, it is probable that, after exposure to infection, some of the virus remains about the person or in contact with the skin for several days or even weeks without producing any effect; but when it passes beyond the epidermic barrier it multiplies rapidly, and within twenty-four hours produces its local specific effect.

Symptoms.—(*a*) *Local.*—The cutaneous lesion is not often seen by the surgeon during the early papular stage. When it proceeds from the bite or sting of an insect, the first symptom is a painful itching at the spot, and within a few hours a red papule with a minute central puncture appears; on the following day a vesicle forms with some surrounding redness, and beyond this considerable brawny swelling. When the top of an ordinary pimple has been scratched off and inoculated at the same time—which is very common—the spot is very irritable and painful; on the second day there is usually a vesicle which may vary in size from a split pea to a shilling, and contains a yellow or brown exudation. On the third day the vesicle has burst and shrunk, leaving a brown base exuding serum. On the fourth day there is a *black, dry, depressed eschar*, surrounded by a very characteristic slightly elevated border of small vesicles. The vesicular rim may be indefinite and irregular, or complete; and other red-currant-like vesicles on the surface of the adjoining skin may be few and discrete, or many, confluent and extensive. The exudation during life is fluid and often very abundant; after death it may not flow out when the vesicles are opened. When the eschar extends by including the earlier vesicles, others form irregularly on the skin around and beyond the margin of the eschar.

When there has been a primary anthrax papule on sound skin there may be no red areola, even after the eschar has formed; but there is always a considerable degree of firm œdema of the surrounding tissues. The purer the poison, the less will be the surrounding inflammation. If the virus be mixed with other irritative material—"mixed infection"—there will be more redness. The firm, unyielding œdema extends in all directions, and the neighbouring lymphatic glands may be tender, hard and enlarged. When the lesion is on the neck, the swelling may, within two or three days, involve the larynx or the mediastinal glands, and produce difficulty of breathing and swallowing, so that fluids taken by the mouth may be returned through the nose. If the lesion be near the eye, the swelling of the eyelids may render the person unable to continue his work, although he may feel quite well. In severe cases the œdema may extend all over the head, neck and chest to below the nipples. The circumference of the head from chin to vertex has been known to reach 29½ inches, and over the eyebrows 26¼ inches. The general absence of pain round the eschar is remarkable; it is never acute, and is rather a sense of weight, fulness and numbness in the part due to the swelling. There is always an entire absence of pus till after ten to fourteen days, when the eschar begins to separate in the ordinary way.

(*b*) *General.*—The severity of the general symptoms bears no relation to the amount of local disease; a small pimple on the neck or chin, without much pain, inflammation or œdema, may be fatal within five days. On the other hand, an eschar on the temple, with large bullæ above, freely discharging straw-coloured fluid, with swelling all over the head, and involving the submaxillary glands, may terminate in recovery. In a case seen by myself, on the seventh day after accidental inoculation of the forearm, the whole of the arm was very much swollen up to the shoulder without any redness, and without change of the pulse or temperature, or the patient feeling ill; yet a fatal result followed on the ninth day. In a few cases with considerable local lesions there are no general symptoms, the patient being able to eat, sleep, and go about as usual; in other cases there is but a slight feeling of illness. In more severe cases the symptoms of general infection occasionally set in with the appearance of the pimple; at other times they may be deferred for a week or more. The initial symptoms are those of any other febrile disease; such as slight feeling of illness, weakness, chilliness, occasionally a slight rigor, some thirst, at times vomiting, fulness in the head, restlessness, and disturbed sleep. The symptoms afterwards appear according to the internal localisation of the disease; this may be in the stomach, with persistent vomiting; in the bowels, with troublesome diarrhœa; in the lungs, with rapid breathing and a tendency to cyanosis; in the brain, with delirium, convulsions and coma; in the heart, with rapid collapse and death. During the first few days the pulse may not be affected; but as the state of the patient becomes more grave, it will be small, rapid, irregular, weak, and ultimately imperceptible. For several days there is usually no fever, and later the temperature is not commonly over 102° F. In the rectum it is generally 3° to 5° higher than in the axilla. It has been noticed to be 104·6° in the axilla shortly before death. In one case it reached 105·1° in the rectum, and yet recovery followed. In some fatal cases, when the brain and meninges were involved, the temperature ranged from 103° to 106°. Occasionally the temperature falls before death.

Diagnosis.—The occupation of the patient may sometimes afford a clue to the nature of the disease. In the earliest papular stage, if the patient had been exposed to infection, a pimple on any uncovered part of the body would excite suspicion; in other cases a positive diagnosis would be impossible. The vesicular stage is more characteristic. The exudation may be clear and straw-coloured, or brown. Redness, swelling, and tenderness may extend along the lymphatics to the neighbouring glands. All these signs, however, may be present and yet anthrax be absent. A positive diagnosis may be made directly by microscopic examination of the fluid for the bacillus anthracis; or indirectly by inoculating a white mouse with a drop of serum from a vesicle. If it be anthrax, death of the mouse will follow within two days, and some of its internal organs will be found crowded with the bacillus anthracis; or a pure cultivation may be obtained on gelatine or other suitable medium, and examination of the culture will decide the diagnosis.

After the lesion has been extending for three or four days, the central early eschar, with surrounding vesicles, redness, extensive œdema and but slight pain about the part, will be very characteristic. It may be distinguished from a boil or carbuncle by the absence of suppuration, and also by the absence of the moist, yellow, sloughing core; from phlegmonous erysipelas and cellulitis by the absence of pain: and, although these may be attended with vesication and gangrene, the gangrene is more extensive, the vesication is not on the margin of skin surrounding the eschar, and the œdema is not so sharply defined; from chancre by the rapidity of its progress and the more serious constitutional symptoms; from glanders by the absence of the numerous red vesicles and the copious puriform discharge from the nostrils; from malignant œdema—progressive gangrene of the skin—by the absence of crepitation of fœtid gas in the cellular tissue, and by cultures and inoculations.

Prognosis.—The danger to life cannot be estimated by the extent of the local disease. A lesion on the cheek the size of a split pea with very slight redness and swelling has been known to lead to a fatal result within four days; yet a larger lesion with extensive œdema and involving the glands may end in complete recovery. The most dangerous site of the local lesion is on the neck, on account of its proximity to the larynx and mediastinal glands; the accompanying œdema and hæmorrhages involving vital organs. From the report of Dr. Hamer to the London County Council on cases of malignant pustule in London (1873-93), mostly treated at Guy's Hospital, it appears that of 38 cases, in which the charbon was seated on the neck, about 40 per cent were fatal; while of 77 cases, in which the lesion was on other parts of the body, 12 per cent were fatal. When the lesion is situated on the upper part of the face the exudation is sometimes very abundant. This may trickle into the mouth, set up vomiting, and increase the danger from secondary intestinal infection. Active reaction with much inflammation around the lesion is generally a favourable symptom; but redness may be absent and the patient recover: on the other hand, it may be very considerable and the patient die. So far as the bodily temperature may have prognostic value, it is more favourable when high than when subnormal. A decreasing temperature with an increasing gravity of general symptoms is a precursor of death.

Delirium is not a common symptom; when it does occur it is of a very serious import, as it generally indicates hæmorrhages between the arachnoid and the pia mater.

Vomiting is not of great importance at the outset, but later, if persistent, it indicates general infection. Diarrhœa is rare during the local stage of the disease; afterwards it is occasionally troublesome, and indicates general infection with concentration of the effects of the virus on the digestive tract. Respiration over forty a minute also indicates localised internal presence of the bacillus anthracis, especially if the cough be troublesome. The pulse is perhaps the best guide to the condition of the patient: so long as it is full and not very rapid the case is hopeful; but when small, feeble, and increasing in rapidity on each visit, it is of serious import. The pulse, temperature, and respiration may, however, be near normal, and the patient not complain of feeling particularly ill, even on the day preceding death.

Duration of Illness.—Number of cases fatal within

2 days.	3 days.	4 days.	5 days.	6 days.	7 days.	8 days.	9 days.	Over 9 days.	
2	3	12	6	11	10	5	5	1	—Total 55

Mortality.—The 11 cases recorded by Dr. Budd (1863) were all fatal. The less serious cases at that time, and for many years afterwards, were not recognised as anthrax. Dr. Russell (1879) gave 4 cases, 3 of which were fatal. In the Bradford district 1880-94, 27 cases have been noted, 13 of which were fatal. Of the 114 cases collected by Dr. Hamer (1873-93), mostly of workers employed in the hide and skin trade who were instructed as to the serious nature of the disease and the importance of early treatment, 21·9 per cent were fatal. Dr. Muskett, South Africa, treated 50 cases without a single death. Dr. Woolmer, Argentine Republic, had 40 cases, with only 1 death. He wrote later: "I have probably had nearly 500 cases of malignant pustule and remember only to have lost two." It is not improbable that the greater heat, light, and activity of septic organisms in these countries lessen the virulence of the anthrax bacillus.

Treatment.—From the earliest times all writers on the treatment of anthrax have recommended the destruction of the primary focus of infection by caustics or cauteries. The actual cautery is still the chief treatment in Russia, Persia, Western Asia and South America, the countries where the disease is most prevalent.

In England, following the practice at Guy's Hospital, where the disease is most frequently seen, excision with the knife is preferred. We must bear in mind, however, that although the disease generally declines after excision, it sometimes develops more rapidly immediately afterwards; and also, that when the œdema is so extensive or so situated that removal of the affected part is impracticable, the disease may recede and the patient recover. Yet notwithstanding the risk of increasing the danger, excision of the local lesion should, if practicable, be performed at the earliest possible moment, and tissues removed at least half an inch beyond the limits of the eschar. During the operation the wound should be irrigated with a 5 per cent carbolic lotion. When the bleeding has been arrested the raw surface should be swabbed with a 10 per cent solution of carbolic acid in equal parts of water and ether. It is also advisable to inject into the tissues around and beneath the wound at one inch distance, and in half-a-dozen places, 15 minims of a 5 per cent solution of carbolic acid in equal parts of water and ether. A compress of this solution should be applied over all, and on this an ice-bag. A solution of mercuric biniodide—made by dissolving mercuric perchloride gr. v. and potassic iodide gr. xx. in 10 oz. of distilled water—may be used in the same way for hypodermic injections to the extent of two drachms of the solution each time. These local injections, which are also intended to affect the general condition of the patient, must be repeated every four hours if the symptoms are urgent; and less frequently when they are relieved.

2. INTESTINAL ANTHRAX—*Mycosis Intestinalis.*—In man general infection by food or water through the digestive tract is very rare. The first case recorded was by Wahl in 1861. In the tissues Virchow (46) found "fine vibrios," which he considered were probably present before

death. In 1864 Recklinghausen noticed a similar case. In 1868 Prof. Buhl described cases where after death hæmorrhagic infarcts were found in the stomach and intestines very like the lesions seen in the bowels of horses dead from splenic fever. He also stated that small thread-like rods swarmed between the corpuscles of the blood. In 1871 Waldeyer met with such cases, and discussed the anthrax origin of the attacks without arriving at any satisfactory conclusion. Dr. Munch of Moscow, in 1871, was the first who determined the anthrax nature of this disease which he had found in hair-workers with internal lesions similar to those noticed by von Wahl and Buhl. Since then cases have been recorded by Wagner in 1874, Albrecht in 1878, and Kelsch in 1881. Many of these, however, were cases of pulmonary anthrax, with secondary intestinal infection.

Ætiology.—The active morbific agents in the flesh meat of animals which have died from anthrax are mostly in the form of bacilli and also of spores which have formed on or near its surface. These are generally destroyed by cooking; if some escape they are attacked by the gastric juice in the stomach. Some spores may escape both these destructive processes, and pass into the intestines, where they may become attached to the epithelium, germinate, and by some defect in this protective lining, or otherwise, may find their way into the circulating blood or lymphatics, and produce disastrous effects by the toxines which they produce.

Man is not very susceptible to this form of anthrax. No such case has been recorded in this country,[1] although they are not uncommon in countries where the disease is very prevalent. It has often happened, when a butcher has contracted the external form of the disease, that the carcase of the animal had been distributed and eaten before the dangerous nature of the accident had become known; yet district registrars' returns of deaths when examined have given no indication of injurious consequences. Still the eating of such meats is dangerous, as the virus may be introduced through an abrasion of the mucous membrane on the lips, the tongue, or other parts of the alimentary canal. Many cases of reported infection by milk, whey, butter and wearing apparel have not been proved to be due to these, or indeed to be anthrax.

The Symptoms are those of poisoning of a gastro-intestinal character, with or without those of a febrile attack, and develop rapidly into those of general infection as seen in other forms of anthrax. There may or may not be, firstly, slight febrile symptoms—such as pain in the head, back, and limbs—with nausea, persistent vomiting, abdominal pain and diarrhœa, which is sometimes hæmorrhagic. The patient feels very weak, helpless and restless; the pulse is small and rapid; the temperature in the rectum a little above normal; the surface of the skin cold and moist, the respiration rapid, and the face slightly cyanotic; the blood stagnates in the extremities, and occasionally convulsions and coma are followed by collapse and death in from two to five days.

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[1] The case published by Dr. G. N. Pitt (35*a*) and that recorded in the post-mortem records of Guy's Hospital (Aug. 1889) were cases of primary cutaneous anthrax. In Dr. Pitt's case the infection was on the left cheek, and the stomach œdema was part of a general infection. In the Guy's case there was also on the cheeks "much œdema, vesicles diffused, but not typical pustule with central slough."

Diagnosis.—The occupation of the patient may give an indication of the nature of the illness. The progress is so rapid, and the symptoms so like other cases of gastro-intestinal specific poisoning, that a definite diagnosis during life may be impossible. If the virus have been introduced through an abrasion of the mucous membrane before reaching the stomach it may cause much œdema of the surrounding tissues, and about the root of the neck externally. In such a case bacilli anthracis have been found in the serum before death. No case demonstrated during life to be intestinal anthrax has ended in recovery.

Treatment.—If it were known that the patient had ingested anthrax material, non-toxic germicides would be the best remedies, such as salol gr. x., or β-naphthol gr. xv. Perhaps the mercuric perchloride or biniodide solutions with brandy might be useful.

3. PULMONARY ANTHRAX—*Wool-sorters' Disease, Anthracæmia.*—It is probable that anthrax in the three forms now recognised has afflicted mankind as long as the disease has prevailed among domestic animals. Since the year 1713 it has been known that persons who handled particular kinds of hairs and wools often suffered from "malignant carbuncle"; and more recently it has been found that they are also liable to outbreaks of a rapidly fatal disease which is ætiologically cognate with splenic fever in cattle.

Doubtless some of the cases described by Dr. Stone and Dr. Hodges among the hair-workers in a factory at Walpole, Massachusetts (1853-70), were cases of this kind; Drs. Neyding and Munch (34), Moscow (1871), Dr. Wagner, Leipzig (1874), and Dr. Russell, Glasgow (1879), recorded similar cases which occurred among workers in hair or bristle factories, and were named "mycosis intestinalis" or "internal anthrax"; although some of them were pulmonary in character. Since 1870, according to Eppinger (13), numerous cases of a similar disease have been observed among rag-sorters in Lower Austria and in other countries. In 1877 Professor Kundratt in two cases found bacilli similar to those of anthrax. In 1878 Frisch proved experimentally that some cases were anthrax, others appeared to be caused by the bacillus of malignant œdema, others again by the bacillus proteus hominis. The only case of pulmonary anthrax in a rag-sorter which has been noticed in this country was reported by Dr. S. Lodge, jun., in 1890.

The disease was first noticed in the Bradford worsted district after the introduction of alpaca and mohair as textile materials in 1837. Occasional unusual illnesses and sudden deaths occurred among the sorters of these "wools." At Queensbury in 1846 several deaths occurred within a short time. Again in 1853-4 there was an outbreak of this disease which caused considerable alarm. In 1867-8, and again in 1874, many deaths of wool-sorters occurred at Saltaire where alpaca and mohair were largely used. Eminent medical and scientific gentlemen made examinations, analyses and reports without satisfactory results. In June 1877 I attended an alpaca-sorter who was at his work in the morning, and was dead at night; after seventeen hours' illness. It was evident to me that he had not died from any ordinary disease, and investigations were commenced in the hope of finding out its nature; other cases occurred, and were carefully inquired into, until, in Nov. 1879, when attending such a patient—who died twelve hours afterwards—I took some blood from the arm, and within a few minutes I injected two or three drops of it under the lumbar skin of a rabbit, a guinea-pig, and a white mouse respectively. The animals all died within sixty hours, and the blood of each showed the presence of bacilli. Another animal was inoculated with blood from one of these, and it died in a shorter time. The fluids from this animal were found to be crowded with bacillus anthracis, and the disease was recognised as anthrax.

During the year 1880 Mr. John Spear, with whom was associated Professor Greenfield, made an exhaustive report on behalf of the Local Government Board on "Wool-sorters' Disease as observed at Bradford and in neighbouring Districts in the West Riding of Yorkshire." This report conclusively proved the disease to be anthrax due to the presence of the bacillus anthracis in the blood and organs of the body.

Ætiology.—This form of anthrax may attack any person exposed to the inhalation of anthrax spores in dust arising from the products of diseased animals. The disease has been known to attack wool-sorters, rag-sorters, packers, washers, carders, combers, overlookers, buyers, manufacturers and others who come in contact with the material before its manufacture into textile goods is complete. Women are seldom attacked, as they are not employed in these processes of the worsted industry. In the rag-picking of the paper industry in Lower Austria, and in the epidemic reported upon by Dr. Russell in Glasgow which occurred in a horse-hair factory, the victims were women.

Wools and hairs are more or less noxious according to their dryness or greasiness, and contamination with diseased animal products. Wool from sheep is pervaded by a peculiar kind of unctuous substance or natural potash soap which is called "yolk." This protects the animal from rain and cold, and also nourishes the wool, rendering it soft, oily and pliable. It is equal in weight to 7 or 8 per cent of the wool. British, Irish and Colonial wools, and also foreign wools, even from countries where anthrax is very prevalent and containing contaminated fleeces, if they are "yolky," are not injurious. Dampness and greasiness fix the dust and virus, and render them almost innocuous. Cutaneous anthrax is occasionally caused by these wools, but never the pulmonary form. Asiatic, Egyptian and other low-class wools from warm climates have not much "yolk"; they are dry, dusty and dangerous. Mohair from the goat of Asia Minor and the Cape has very little "yolk." Sheep and goats in these countries are often herded together, and are equally liable to anthrax; yet the wool from the sheep containing "fallen fleeces" will be almost innocuous, whereas the hair from a goat equally contaminated will be dangerous. Hair from the alpaca, llama, vicuña, camel, horse and cow, has no yolk. On this peculiarity depends very much the difference beween dangerous and innocuous wools and hairs.

The sorting of wools and hairs is unhealthy in proportion to the contamination they produce in the air inspired by the worker: 1st, The dust and fine short hairs, acting mechanically, excite chronic diseases of the lungs, such as bronchitis and phthisis; 2nd, Septic poison dust from dried decomposed animal matter produces a low form of septic pneumonia; 3rd, The virus arising from the blood and discharges of animals that have died from anthrax acts specifically on the lungs. No case of primary intestinal infection or of anthrax œdema without lesion of skin has been observed among wool-sorters. Periodic outbreaks among work-people are probably dependent upon epizootics of anthrax in the countries from which the material has been obtained.

The proportion of external to internal forms of the disease varies in different industries. In the Bradford worsted district 30 cases of external and 57 cases of internal anthrax have been recorded. In the London hide and skin trades 90 cases of external and only 2 of internal have occurred. Among the rag-pickers of Lower Austria 89 cases were all of the internal kind. Doubtless many cases of all kinds occur which are not diagnosed as anthrax.

Symptoms.—The aspect of the disease is really negative. There may be no rigor, pain, cough, vomiting, purging, or other distressful condition until the near approach of death; even then the patient may not feel particularly ill. For example, a previously healthy mohair-sorter, aged 46, not feeling very well, called to see his doctor at 10.30 A.M.; during the afternoon, when taking a walk, he noticed his hands were cold and his finger-nails were of a bluish colour. He had a restless night, his breathing being oppressed and rapid, and he died at 10 A.M. Duration, twenty-four hours. A Van mohair-sorter, aged 23, when taken ill, wished to be removed to his parents' home eight miles away. He said he felt "all right." Against the advice of his doctor he went, and died in the cab on the way. Another Van mohair-sorter, aged 39, got up and dressed himself to go to work as usual, but feeling weak he went back to bed, and died at 5.30 P.M. the same day. A strong healthy man, aged 39, after a moderately good night, got up at 6 A.M. to go to work, his hands and feet were cold, he fainted, got into bed again, and died at 2.30 P.M. the same day. An alpaca-sorter, not feeling very well on a Saturday, thought the fresh air at the sea-side, 120 miles away, would do him good. On Sunday afternoon he had a short walk in the garden, was worse during the evening, and died early on Monday morning.

Prodroma.—The sorting of dry, inferior and damaged wools and hairs produce in most men "difficulty of breathing," oppression and "tightness of the chest," and "cough." These effects are more felt when bales containing "fallen fleeces" are opened; they cannot, however, be considered prodromal symptoms of anthrax, and are probably due to other impurities.

Initial.—These, in unmixed cases, are common to many diseases; and are never severe or painful. The patient feels "out of sorts," "not well, not ill," "not half well," "as if he had caught cold and something was coming on." In 21 per cent of cases there is shivering — not amounting to a rigor; in 25 per cent a slight chilliness, in most cases some uneasiness at the chest or stomach, and in all cases great weakness and weariness. The distress, however, is so slight that the doctor is not summoned till one, or more frequently two days have passed; when the patient, without his feeling seriously ill or his friends being apprehensive of danger, may be found in a collapsed condition, cold, almost pulseless, and within a few hours of death.

Alimentary System.—The tongue is always moist and generally coated with a slight creamy-coloured covering. Thirst is usual, in a few cases extreme. Appetite is not good, but some have partaken of food moderately after leaving work ill; there may be nausea, weight and uneasiness at the stomach. Vomiting is mentioned in 43 per cent of the cases; this may occur once only in the early stage of the disease, and is unimportant; in other cases it may be persistent, commencing after the second day, and depending upon concentration of the disease upon the stomach and bowels. Diarrhœa is not so frequent as vomiting, it occurred in 10 per cent of the cases with occasional abdominal pain; bloody evacuations have not been noticed.

Respiratory System.—The lungs are always involved, although occasionally the symptoms are slight. In 5 per cent of cases there is pain in the side, but it is seldom severe or continuous. Nearly all have a feeling of tightness, oppression, weight or pressure about the chest which interferes with the breathing. In some this is the only chest symptom. The breathing is accelerated, difficult, and in the later stage forty to fifty a minute; but in two cases, when the patients were cold and almost pulseless, the respirations were only twenty-five and twenty-six respectively. Cough is generally present, but never severe or very troublesome; in 14 per cent of cases there was no cough, in 22 per cent it was very slight or short. In most cases there was no expectoration, in none was it very much; occasionally it contains numerous small specks of blood, and in a very few, and only in cases which had continued over five days, was it rusty-coloured.

The purer the case, the less likely is there to be any pneumonia. The breath has often been noticed to have a faint, sickly, peculiar fœtid odour. A dusky leaden hue or lividity of face, neck, ears and fingers, increasing to cyanosis in the collapse stage, is usual.

Percussion sounds are generally clear; occasional impairment has been noticed on either side, but generally on the right; it is never very decided, even when the examination has been carefully made a few hours before death, although much fluid has been found in the pleural spaces at the post-mortem examinations.

The respiratory murmur on the right side is feeble during the early stage, and may be inaudible over the upper half or more of the lung at a later stage—the percussion note being clear—from pressure of enlarged glands on the bronchi. Dry, sibilant, cooing sounds are common on this side; moist, bronchial râles may be present, but crepitations are very rare. The left lung is seldom affected so much as the right, and much less frequently. Some dulness and crepitations have been noticed in exceptional cases.

The Circulatory Organs.—In some cases the force of the virus appears to fall more upon the heart than on the lungs. Generally the pulse is soft, small, weak, rapid and irregular; according to the stage of the disease. At the commencement the frequency and force of the pulse may not differ from the normal, so that danger may not be suspected. In the rapid case (see p. 544) the pulse was 100 a minute seven hours before the patient's death; in another case, twelve hours before death, it was only 82. It is, however, usually weak and rapid out of proportion to the apparent severity of the illness (120 to 140), and as the patient approaches the end it becomes very small, irregular and uncountable. The heart sounds are also very feeble and at times inaudible.

The Nervous System.—21 per cent complained of headache; rambling of the mind and delirium occurred in 22 per cent, of which number five became comatose, and three had convulsions. In most of these the virus seemed to settle upon the brain, producing meningeal hæmorrhage. Four of the cases had lasted over five days; and the symptoms might be due, for example, to secondary blood changes from pneumonia. In 78 per cent the mind was clear throughout the illness.

Skin and Temperature.—The skin is always moist, and in many patients, when the surface of the body is cold, it is bathed with perspiration. The temperature in the axilla in ordinary cases seldom reaches 103°; the few cases in which 104° to 105° have been recorded were prolonged and combined with pneumonia: in one case 107° was noted two hours before death on the seventh day. The temperature is usually 4° to 5° higher in the rectum than in the axilla, and falls as the disease advances; as in the following examples—seven hours before death, axilla 97·6°, under tongue 98·1°, within rectum 102·2°. Another: axilla 96·1°, under tongue 99·5°, within rectum 103·1°; five hours afterwards, when cold and pulseless, rectum 101·7°. Again, twelve hours before death, axilla 97·2°; shortly before death, axilla 93°, rectum 101°. In another two hours before death, axilla 99·2°, rectum 104·2°.

Urinary System.—The urine is scanty, dark-coloured, and of high specific gravity, even up to 1040. In several cases, both of the cutaneous and pulmonary form, it has been found to contain albumin—in one case equal to two-thirds of the bulk operated upon. More frequently it contains but a small quantity, and in the greater number of cases not any. In one case of cutaneous anthrax, in which the patient recovered, the specific gravity was 1043, and a quantity of sugar was present.

The symptoms and progress of pure cases are what we may suppose would follow from the inoculation of virulent anthrax virus into the circulating fluids of a healthy person. In the most rapid cases the invading force is so overwhelming that the initial collapse continues, and the strong man yields his life without a sign of resistance. In ordinary cases reaction takes place, followed by collapse and death before local inflammatory lesions mask the nature of the illness. In more prolonged cases inflammatory changes take place in the lungs, which very much obscure the nature of the illness, and add their own particular dangers; but they indicate a diminished risk from the anthrax poison.

Rapid Case.—R. N., aged 58 years, married, strong, stout, and healthy-looking, had been a wool-sorter over forty years. His previous health had been good, he had also been very regular and temperate in his habits. For fourteen years he had sorted alpaca. On June 25th, 1877, he had opened a bad bag. The following morning when at his work he felt weak and perspired freely. He had great difficulty in walking home, two and a half miles. He went to bed directly, and, as the breathing was rather oppressed, took an emetic of mustard, salt and warm water. He was seen by me at seven o'clock the same evening, and stated that he had not felt chilly; there had been no thirst, vomiting or pain; the tongue was moist, slightly coated, and felt cold to the touch; there was some wheezing in the trachea, very little cough, no expectoration; respiration 34, no dulness on percussion of chest, some dry cooing sounds over right lung posteriorly, no moist sounds; pulse 100, very weak and irregular; temperature in axilla 97·6°, under tongue 98·1°, within rectum 102·2°. At 11 P.M. there was no dulness on percussion of chest; respiration 40, no moist sounds, dry sounds on right side; temperature—axilla 96·6°, rectum 102·5°; pulse rapid, irregular, uncountable; hands, knees, face, and tongue cold; perspiration free, mind clear. He died three hours afterwards. Duration, seventeen hours.

Ordinary Case.—S. F., aged 35, a sorter of mohair, on May 3rd, 1880, complained of feeling rather sick and weak; he had no pain, slight cough, no expectoration. Chest on percussion in front and behind clear, respiratory murmur over right lung very feeble, no moist sounds, respiration 24; pulse 126; temperature, axilla 100·4°. There was nothing apparent in his general condition to cause or correspond with the dangerous character of the pulse. *May 4th.*—Had little sleep; respiration 28; pulse 120, small, feeble, and uneven; temperature—axilla 98·1°, mouth 100°, rectum 102·4°. Complained of nothing but sickness, had vomited frequently; at 10 P.M. right lung sounds very feeble, no decided dulness, respiration 30; pulse 116, very weak; temperature—axilla 97·3°, mouth 97·9°, rectum 101°; extremities cold. *May 5th.*—Lungs resonant, no crepitations, respiration 40; tongue moist; pulse 120, scarcely countable; collapse increasing; temperature—axilla 97°, mouth 98°, rectum 100·8°. At 5 P.M. the lungs anteriorly were resonant, respiration 48; pulse almost imperceptible; very restless. At 8 P.M. he died. Duration of illness, four days. Large numbers of typical anthrax bacilli were afterwards found in the blood.

Prolonged Case.—M. C., aged 30, a Cape mohair-sorter, had always had good health. He left work on May 19th, 1880; felt shivery, as if he had an influenza cold; perspired freely; slight cough; temperature 103°, pulse regular, full, 128. On the 20th had pain in the left side, felt weak, perspired freely, slight rusty expectoration; some crepitations at the base of left lung posteriorly, no marked dulness; temperature 104·2°; pulse 128. On the 22nd passed a restless night; no cough or expectoration. On the 23rd felt nicely; no pain. On the 24th more pain, particularly in chest. Tubular breathing over lower portion of left lung posteriorly, dulness marked, also slightly on right side; temperature 103·2°, pulse regular, 130. On the 25th felt better; not much pain; mind wandering. On the 26th appeared better; not much cough, some expectoration, not coloured; sat up in bed when doctor was present, and took a pint of mutton broth. On the 27th much worse, insensible; breathing laboured and rapid; pulse 136, weak and irregular. Hands and arms warm. He died shortly afterwards. Duration, nine days. Characteristic bacilli were found in the pericardial serum.

Duration of Illness.—Number of cases fatal within

1 day.	2 days.	3 days.	4 days.	5 days.	10 days.	Over 10 days.	Total.
3	13	18	13	7	7	2	63

Diagnosis.—The slightest illness occurring in those exposed to infection should be looked upon with suspicion, until the possibility of it being anthrax has been negatived. In the early stage, when the symptoms are the same as those of ordinary ailments, diagnosis is impossible. In the middle stage there is often nothing characteristic in the condition of the patient to determine the grave nature of the disease; hence not infrequently it is unrecognised until the patient is cold, livid, almost pulseless and dying. In the last stage of rapid or ordinary attacks the combined symptoms, as before given, are sufficiently definite. In the more prolonged cases, complicated with pleurisy and pneumonia, diagnosis is very difficult and uncertain; perhaps a weak pulse and prostration out of proportion to the local lesions may excite a suspicion, which can be confirmed or dispelled by bacteriological or physiological methods only. The microscopical examination of the blood for bacilli will not often be conclusive; it is, however, reported that bacilli have been found in the blood of patients who recovered. When the nature of the disease is apparent, bacilli may or may not be found in blood taken from the finger or lobule of the ear; and this blood if given subcutaneously to a mouse will certainly be fatal.

Prognosis.—When a strong man, a sorter of noxious material, complains of slight illness, as if he had got cold, and after careful examination nothing more is apparent, a guarded prognosis must be given; he may be dead within twenty-four hours.

If the onset be more decided, and there has been shivering, followed by other symptoms of a "severe cold," and a temperature above 102·5°, the prognosis will be more favourable; these symptoms indicate that the patient has been able to resist the onslaught of the specific disease: and, although broncho-pneumonia, pleuritic effusions, and secondary suppurations may follow and add their own dangers, these complications are antagonistic to anthrax development, and the chances of the patient's recovery are more favourable.

It is probable that many patients recover from attacks of this disease, as they do from cutaneous anthrax. Animals recover from severe attacks of constitutional anthrax produced experimentally. But although bacilli have frequently been found in blood taken from patients several hours before death, in a few only have they been seen in the blood of patients who recovered; indeed in no recorded case of recovery has their presence been proved by accurate experimental methods.

PATHOLOGICAL ANATOMY.—**Cutaneous Anthrax.**—*Local.*—Davaine (11), Wagner, Koch (26), Cornil, Straus, and Turner have described the states present at different stages of the disease. During the first few days the changes in the skin at the point of inoculation are those of acute inflammation, followed by fibrino-serous exudation and central necrosis. The black eschar, consisting of epidermis including the Malpighian layer, is depressed, and does not extend deeper than the skin. The epidermis around may be detached, and the dermis appear of a dirty yellow gray, or a reddish purple colour. The exudate contains red blood globules, a few leucocytes, the bacilli anthracis, and often other accidental microbes. The papillæ are swollen, and the interspaces filled with leucocytes and bacilli anthracis. The bacilli are irregularly distributed, but are most numerous near the eschar, beneath the adherent epithelium in the Malpighian layer. In the surface layers of the skin, after a few days, other bacteria are found. In the deeper layers there are very few bacilli, they do not extend in great numbers more than two inches beyond the eschar. They are not found in the adipose tissue beneath. The brawny swelling when cut may be crowded with small interstitial hæmorrhages.

General.—The states of the various organs are in great measure similar to those found after death from all forms of anthrax, the local lesions predominating according to the part inoculated.

Intestinal and Pulmonary Anthrax.—*External Changes.*—The discoloration of decomposition appears very soon; it is of more than the usual lividity, and is not confined to the posterior parts of the body. Within two to four hours the lips, ears, neck, upper part of the chest, and shoulders are of a dark purple colour; the nails of a black-blue colour, and the exposed skin of the penis and scrotum claret-coloured. There may also be minute purple spots on various parts, more frequently on the chest and abdomen. Dark chocolate-coloured fluids issue from the mouth and nose. The cellular tissue in front of the neck and upper part of the chest is sometimes swollen and emphysematous, and gives a crackling sensation under the finger on pressure.

Internal Changes.—The external muscles of the chest on section are often dark-coloured, except where there is much œdema. On removing the sternum the cellular tissue beneath is sometimes emphysematous, and bubbles of gas escape; at other times there is found—not infrequently—considerable gelatinous œdema of the cellular tissue; occasionally it has been seen to be extensively infiltrated with blood. The pleural spaces almost invariably contain a large quantity of clear, straw-coloured serum; often two to four pints in each side—generally most in the right side. Any inflammatory lesions of the pleuræ are due to accidental causes. The anterior surface of the lungs may appear normal; or the gelatinous œdema under the serous covering may be as much as one inch in thickness at the most dependent parts, and may extend between the lobes without any plastic inflammatory exudation. Under the serous coat are often numerous small patches of ecchymoses. On section the lungs are engorged with dark-coloured blood, the right more so than the left; the posterior and lower parts are more congested and œdematous; some portions are more solid than others, and of a blacker red colour. It is not uncommon to find extravasations of blood — any size to that of a walnut — in the parenchyma of the lungs; and in prolonged cases the larger of these appear to become puriform.

The Bronchial Glands are generally enlarged—not invariably; they may be the size of a hen's egg. The right is usually the larger. They are hard, easily broken down by the thumb, and filled with dark-coloured blood. The Trachea and Bronchial Tubes contain frothy, blood-stained mucus; the mucous membrane of the trachea and of the larger bronchi is stained a claret colour and swollen; beneath it patches of extravasated blood are frequently seen. On a transverse section the lumen is seen to be narrowed by jelly-like, sero-sanguinolent, and hæmorrhagic infiltration. The pharyngeal connective tissue may be œdematous and infiltrated with blood.

The Pericardium at its base may be surrounded by blood diffused in the cellular tissue. It may have numerous petechial spots between its layers, or they may be separated by a thick layer of gelatinous serum. The pericardial fluid is frequently increased in quantity up to five and six ounces. The Epicardium and Endocardium show subserous petechial patches, those within the heart at the attachment of the valves being the largest.

The Blood is nearly always fluid and of a dark colour, almost black. n a few prolonged cases soft clots were found in both ventricles. The uid blood produces swelling and engorgement of the parenchyma of the ternal organs.

The Heart Muscle is dark-coloured, soft and flabby; it may be empty, contain dark, semifluid blood in all its cavities. The auricular and ntricular septa, and parts of the muscular substance, may even be of black-red colour from extravasations or staining of blood. The attachents of the cords to the muscular columns of the tricuspid and mitral valves may be similarly discoloured. A dark red, even layer of blood may separate the serous layers of some of the cusps of the pulmonary or aortic valves. The corpora Arantii may be seen black from ecchymoses. The lining membrane of the heart and larger vessels is stained with a hue varying from a pale cherry red to a dark chocolate, according to the length of time which may have elapsed since death.

The Abdomen in pulmonary anthrax does not often contain much fluid; but in the intestinal form a considerable quantity may be present. In one case of cutaneous anthrax, on the cheek, serum from which had got into the mouth, the intestines were very much involved; and four pints of blood-stained serum were found in the abdomen.

The gelatinous œdema noticed in the chest is often found in the abdomen; it may be very considerable in the mesentery, or in the cellular tissue surrounding the kidneys. Extravasated blood in small or large patches may be found under the serous covering of the various organs. Between the layers of the mesentery patches as large as the outspread hand have been seen. There may be much blood also in the cellular tissue around the kidney. When the intestines are affected the mesenteric glands may be much enlarged; in other cases they may be normal. In the Stomach and Intestines patches of extravasated blood are found under the mucous membrane, and also numerous large congested patches of a mulberry hue several inches long, and often involving the greater part of the circumference of the bowels; or the ecchymoses may be very numerous, small, each with a black centre, and varying in size from the head of a pin to a lentil. The submucous hæmorrhages when large appear as subserous on the external aspect of the bowels. In other cases the mucous lining of the stomach and intestines may be perfectly normal in appearance.

The condition of the Spleen, like that of all other organs in this disease, varies very much. It is generally larger than natural—half as large again or double the natural size; but not infrequently it is unaltered in size or appearance. When cut into, if much enlarged, it is diffluent, grumous, and the matter flowing out is almost black. In other cases the organ is soft, pulpy, and in appearance as in other specific febrile diseases.

The Liver is less frequently affected than other organs; it appears generally to be normal; but it may be very full of blood; it sometimes presents numerous small hæmorrhagic areas.

The Kidneys have occasionally small extravasations of blood beneath the capsule; the parenchyma is usually gorged with blood.

The Brain and Spinal Cord.—Extravasations of blood not infrequently lie between the membranes, sometimes completely surrounding the brain and filling the lateral ventricles; small infarcts to the size of a pea may occasionally be seen in the cerebral substance.

The characteristic changes are—(i.) The discoloration of the skin: from this alone in many cases the cause of death may be surmised. In some cases, however, it is not decidedly marked. (ii.) The gelatinous œdema of the cellular tissue in various parts of the body: particularly in the anterior mediastinum, around the pharynx, the trachea, the base of the heart; in the mesentery, the omentum, and the adipose tissue around the kidneys. (iii.) The extravasations of blood: which may be extensive in the chest, the abdomen, and the head in the same patient; or in only one of these places; with innumerable smaller hæmorrhagic areas in any organ or tissue in any part of the body. (iv.) The extensive serous effusions into the pleuræ, pericardium, and peritoneum.

Microscopic Anatomy.—*Pulmonary Anthrax.*—For our knowledge of the microscopical characters of the tissues in this form of the disease we are deeply indebted to Professor Greenfield, who, in his report to the Local Government Board in 1881 on the Wool-Sorters' Disease in Bradford, gave a full and lucid account of his numerous experiments and examinations. From this report we gather that "the lesion in the bronchi presented in various degrees constant and characteristic features, limited almost entirely to the lower part of the trachea near its bifurcation, to the two main bronchi, and in one case only reaching to the first division. In the earliest stage of the process the most superficial layers of the mucous membrane are found to be infiltrated with bacilli, later they are found in scanty clusters in the somewhat deeper layers, still however only in the connective tissue spaces or in the lymphatics. Very speedily, however, there appear two special conditions, viz. hæmorrhage and inflammation." The hæmorrhage may be slight into the sub-epithelial tissue, which then becomes detached; if more extensive, it may involve the mucous and submucous tissue through their entire depth. In the vicinity of the hæmorrhages is a more marked accumulation of bacilli; they crowd the superficial layers of the mucous membrane, and are found in larger numbers in the connective tissue; masses are also found here and there in the lymphatics, and sometimes in the smaller blood-vessels.

Distribution of the Bacilli.—In animals the blood, fluids and tissues sometimes swarm with them; in man they are less numerous. They are always to be found in the tissues near the point of inoculation; they crowd the lymphatics to the nearest glands; and, by plugging the smaller vessels, they give rise to extravasations of blood. They are generally present in the serum from vesicles around the cutaneous lesion; sometimes very few, say one in a score of fields, at other times ten to twenty may be seen in each field. The inoculation of susceptible rodents with serum taken during life from a vesicle near the eschar is generally fatal; but sometimes has no effect. Blood and serum from brawny œdema at six inches distance from the point of infection in the early stage do not contain any bacilli; in the later stage a few may be found. Blood from near the vesicles surrounding the eschar may not hold any bacilli. In the early stage of general infection none will be found in the blood, and injection of the blood into susceptible animals will have no effect. In the later stage a few bacilli will be found in the blood from the ear or finger, and the blood when injected into a guinea-pig will be fatal.

The gelatinous œdema contains a few bacilli, never large numbers. This fluid, when injected into a rabbit, has occasionally been found without effect; usually, however, it is virulent. The serum in the pleuræ, pericardium and peritoneum generally contains numerous bacilli. They may not be found in fluid withdrawn during life or possibly after death; but usually they grow in these pure cultivating fluids after death to a considerable length: if kept in a sealed capillary tube for twenty-four hours these leptothrix filaments will be increased and become convoluted. Bacilli are common in the urine of domestic animals when suffering from this disease. In man the kidneys are not so frequently involved; but when they are, bacilli escape with blood from the capillaries of the glomeruli, and grow to a considerable length in the urine before it is voided from the bladder. In the same way, by rupture of capillaries, bacilli are found in milk; they will pass also, by rupture of vessels, from mother to fœtus through the placenta. They have also been found in the fæces and the sputum; but the report of their presence in the sweat requires confirmation.

In sections of the lungs, heart, liver, kidneys, spleen and other organs, bacilli will generally be found in small numbers; but they may be so few and scattered that in some sections none may appear, occasionally not even in the spleen: in other cases they may be innumerable.

Inoculations with blood withdrawn twelve hours before the death of a patient may produce fatal anthrax in rabbits, guinea-pigs and mice; such, however, would not be the case invariably. When the blood has been abstracted within a few hours of death a fatal result has always followed; although, on microscopical examination, bacilli may not have been found in it. All fluids and tissues which contain the characteristic bacilli, and are fresh when introduced into the blood of susceptible animals, will give rise to anthrax; but if not used for three or four days the effect may be slight or absent.

Preventive Measures.—In nearly all cases of anthrax in man the infection is derived from wools, hairs, hides, and so forth, of foreign origin. In the countries whence these are exported they are well known to be from diseased animals, and might easily be classified separately and specially treated. We have no legal power to prevent the importation of such infective materials; but merchants, through their agents, might do a great deal by insisting upon the separation of "fallen fleeces" and "dead hides" from sound materials. At present any foreign wool, hair or hides may be noxious; and, even when opening bales, there is some risk to workmen if the contents be dry and dusty.

The "precautionary regulations" agreed upon at Bradford specify that noxious wools and hairs, which frequently contain "fallen fleeces," shall be steeped and washed in "hot suds" (soap and water), and afterwards sorted while damp; that others, which are dry and dusty, shall be sorted over "boards" (open wire work) provided with dust-extracting fans. The collected dust must be burnt. All dead skin and clippings, and bags in which noxious wools and hairs have been imported, must be disinfected before they are sold. The sorting-rooms must be disinfected and kept clean. The sorter must not work if he have any sore or cut upon him, and requisites for disinfecting and treating such wounds must be kept in the sorting-room.

These regulations, although only palliative and not thoroughly carried out, have done much to diminish the number of cases of anthrax among the work-people.

If bales of dry wools and hairs were placed in steamers — as is done in the melange printing process — and submitted to a steam pressure of six pounds to the square inch — that is, to a temperature of 230° F. — for a few hours, all bacteria would be destroyed. Whether this process would impair these materials for textile purposes is doubtful; some say that the dirt would be fixed and impair the colour of the material, and so diminish its value. If so, it could not injure the most dangerous kinds of material, which are of a brown colour. Such regulations, however, should be impartially applied to the whole of Great Britain.

Treatment.—It is much to be regretted that in so fatal a disease but little can be done in the way of treatment. The progress of the disease is generally so rapid that, almost before a diagnosis can be made, the patient may be beyond recovery. In the early stage, if the pulmonary form be suspected, perhaps the inhalation of germicides—such as carbolic acid (1 in 20), or mercuric biniodide (1 in 500)—in the form of spray, would be suitable remedies; but as these can only reach the surface of the mucous membrane, and the bacilli have already passed beyond this into the tissues and lymphatics, much benefit cannot be expected. The intravenous injection of a sterilised solution of permanganate of potash or of hyposulphite of sodium might be beneficial.

No antitoxin is known which would be of service when the disease is in progress. The inoculation of vaccines and toxins is an efficient preventive of anthrax. Antitoxins may be curative. A small quantity of the blood-serum from a naturally—relatively—immune animal given subcutaneously to a white mouse or a guinea-pig will protect it from the effects of a minimum fatal dose of anthrax virus. It is also curative. Is it reasonable to suppose that such serum may have some arresting action on the progress of the disease if given after infection by anthrax virus? If this prove to be so, "serum treatment" would be beneficial to persons suffering from anthrax. The serum of a naturally immune animal—as the Algerian sheep, or other sheep—which had also been rendered absolutely immune by Pasteur's method, might be obtained and kept in a dry condition. When required for administration it should be dissolved in "normal saline solution" (common salt one drachm, boiled water one pint) and given by subcutaneous or intravenous injection.

The medical treatment of the more chronic cases, which extend beyond five days, and are attended with fever and the development of inflammatory changes and secondary suppurations in the lungs or elsewhere, must be met by remedies which are considered useful in these complications when they arise from other causes, namely—stimulants, salines, strophanthus, quinine, and strong soups. [See article on "Sick Feeding."]

John Henry Bell.

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J. H. B.

INFECTIVE DISEASES COMMUNICABLE FROM ANIMALS TO MAN

(b) OF UNCERTAIN BACTERIOLOGY

39. VACCINIA 40. FOOT AND MOUTH DISEASE
41. RABIES 41*a*. GLANDULAR FEVER

VACCINIA IN MAN—A CLINICAL STUDY

BY T. D. ACLAND

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BY S. M. COPEMAN

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Division into vaccinated and unvaccinated.
References

VACCINIA

VACCINIA IN MAN—A CLINICAL STUDY[1]

PART I

VACCINIA NORMAL AND ABNORMAL

Introduction.—Vaccinia in man is a communicable disorder arising, except in very rare instances, from the accidental or intentional inoculation of an individual with vaccine lymph. The disease is probably due to a specific contagium (9). It has definite periods of incubation, evolution, and decline; and is characterised by an eruption at the point of inoculation, which eruption has certain well-recognised features.

It is improbable that any more precise definition of vaccinia will be possible, until its origin and affinities are more fully determined than at present. Nor is there anything surprising in this, since similar general definitions have to suffice for all the acute exanthems—such as variola and scarlet fever—the recognition of which depends rather on a given train of symptoms, than on a precise knowledge of the causation of the malady.

In the following pages the expression "vaccinia in man" is taken to denote the sum of the results produced by the inoculation of uncontaminated vaccine lymph, as generally practised throughout the United Kingdom.

The course of vaccinia may be normal or abnormal. It may be called normal when the events, subsequent to vaccination, pursue a certain definite and recognised sequence. The gradations, however, between normal and abnormal vaccination are insensible, and no hard and fast line can be drawn between them; although between the cases which occur at either end of the scale there are wide and striking differences.

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[1] In the following pages frequent reference is made to the various reports and appendices issued by the Royal Commission on Vaccination between 1889 and 1896. To save repetition these volumes are referred to as R.C.V. Final Report; R.C.V. Appendix ix., etc.; the latter contains the papers relating to cases in which "injury or death was alleged or suggested to have been caused by vaccination, or to have been connected with it." Of these cases 205 were inquired into by the medical staff of the Local Government Board, and the abstracts of these reports were prepared for the Commission by Dr. Coupland and myself. Besides these, 421 additional cases were brought to the notice of the Commission; and most of them were investigated by Dr. Barlow, Dr. Coupland, Dr. Luff, and myself. These inquiries extended over a period of seven and a half years; that is, from November 1888 to April 1896. The writer is greatly indebted to those who, often at much personal inconvenience, have given him assistance in investigations which were, in some instances, necessarily prolonged; and he wishes to take this opportunity of acknowledging the help which has been given him, both by the supporters and opponents of vaccination, without which help many of the investigations would have been impossible.

Normal vaccination results from the inoculation of a healthy individual with vaccine lymph uncontaminated with extraneous micro-organisms, or other organised or unorganised products, which, although not infrequently present, are not, so far as is known, in any way essential to the process of vaccination or to the production of immunity from small-pox. Under existing circumstances, it may not be possible, as a rule, to collect lymph entirely free from extraneous organisms (44); but even if this be so, healthy tissues are to a certain extent refractory, and no evil result is to be feared unless the dose of extraneous organisms be sufficient to overcome their resistance. This power of resistance, however, is not the same in all cases, and this variation may probably account for the fact which is sometimes observed; namely, that one or more individuals of a series inoculated with the same lymph, develop inflammatory symptoms—such as cellulitis, abscess, or even possibly erysipelas—whilst in others of the same series vaccination pursues a normal course.

It is sometimes urged against vaccination, that it is impossible by examination of the lymph to determine with certainty what results will be obtained. This objection has some weight, since no ordinary microscopical examination of lymph stored in tubes, will reveal pathogenetic or pyogenetic organisms; and it is doubtful whether lymph, collected in the ordinary way, does not always contain blood corpuscles. The force of the objection is, however, more apparent than real; experience shows that lymph taken from normal vesicles in healthy individuals produces certain definite results in healthy and properly cared for infants; while on the other hand no selection of lymph will remove dangers which arise from the method of vaccination, the circumstances or condition of the child, or the improper treatment of the vesicles: all which factors are found to be far more productive of untoward results than any defect in the quality of the lymph itself.

Normal vaccination.—Under favourable conditions vaccination is followed by local manifestations and general symptoms which, within certain limits, vary according to the strength of the virus used, and the peculiarities and circumstances of the individual. The local manifestations are so well known as to need but the briefest mention.

Period of incubation.—In most cases the immediate effect of the operation is nothing more than that which results from a scratch; but in some children of unusual susceptibility, there is immediate evidence of some slight traumatic reaction, such as swelling and redness of the part, which in the course of a few hours entirely subsides until the end of the incubation period. This stage lasts as a rule for about three days.

Period of eruption.—On the 3rd or 4th day, pale red papules develop at the points of inoculation which, in the course of the next five days, develop into compound vesicles with clear contents, and later, about the 10th day, into pustules; the lymph becoming more and more opaque owing to the multiplication of the cellular elements which it contains. The vesicles are at first fully distended and plump; as they approach maturity they become umbilicated, the centre begins to dry, and a scab is formed which increases towards the periphery, and eventually covers the whole pock. Between the 14th and 20th days the scab falls off, leaving a scar which, dusky red at first, gradually, after some months, becomes white and pitted (foveated). The amount of pitting as a rule varies inversely as the amount of inflammation which has occurred at or round the seat of inoculation (for a further account of abnormal conditions of the scar, see p. 562).

About the 5th day, when the vesicles are beginning to form, a faint blush appears round them. This "areola" becomes more intense about the 9th or 10th day, gradually subsiding with the drying-up of the pocks, which begins about the 11th day. The areola extends from ¼ inch to 2 inches round the pocks, the tissues becoming indurated and painful in proportion to the severity of the inflammation.

This areola, formerly supposed to be an important part of vaccination, varies greatly in intensity, and probably is largely dependent on the kind of lymph used and the method of preserving it. (The alleged relations of the areola to erysipelas will be found discussed on p. 588.)

With the retrogression of the pock and the subsidence of the areola the local phenomena of a normal vaccination are at an end.

Variations in the development of the vesicles.—Although under ordinary circumstances the development of the vaccine pocks proceeds in the manner sketched above, there are frequent departures from the normal course, most of which are of little or no importance; many depend on the condition of the vaccinee and his circumstances, some on causes quite independent of vaccination and easily preventable. No useful purpose would be served by giving details of all the variations from a definitely regular development of the vesicles; but the following table indicates the kind of irregularities which are met with from time to time:—

TABLE showing variations in the development of vaccine pocks.

a. Variations in number	Supernumerary pocks. Confluent pocks round points of inoculation. Generalised vaccinia.
b. Variations in size	Due to coalescence of vaccination vesicles. Due to extension of original vesicles by coalescence of surrounding secondary pocks.

c. Variations in contents	Watery.
	Purulent.
	Hæmorrhagic.
d. Variations in evolution	Acceleration.
	Retardation.
	Abortion.
	Recrudescence.
	Persistence.
e. Variations in involution	Inflammation.
	Suppuration.
	Ulceration.
	Gangrene.
f. Variations in healing and formation of scar.	Delayed healing.
	Induration.
	Keloid.

a. Variations in number.—This subject, which is necessarily of some length, will be more conveniently considered under the heading of generalised vaccinia (*q.v.* p. 569).

b. Variations in size.—Two, three, or four of the compound vesicles resulting from ordinary vaccination, may coalesce to form one large pock, the size of which may be almost indefinitely increased by the development of supernumerary pocks in the immediate neighbourhood of the primary vesicles; an example has been recorded by myself (1) in which the sore on the arm thus produced measured 4 inches by 4½ inches.

These cases as a rule are not serious; with cleanliness and protection of the arm from injury, the sores heal well and quickly.

c. Variations in contents.—Under certain conditions, the most important of which are a cachectic state of the vaccinated child, the use of contaminated lymph, or the improper treatment of the vesicles (*vide* Vaccinal Ulceration, p. 614), the contents of the pocks, instead of being clear and bright at the end of the first week, may be watery and unhealthy, or pus may have formed early, or the contents of the vesicles may be hæmorrhagic: any one of these conditions may be of grave importance.

d. Variations in evolution.—(i.) The development of the pocks may be accelerated by the season of the year—it is more rapid in warm weather than in cold—it is influenced by the idiosyncrasy of the individual, and also by the amount and activity of the lymph used. Their development is also accelerated by the degree of immunity which has been attained by previous vaccinations. Thus Cory (9*a*) found by vaccinating in series, one insertion being made on each of eleven successive days, that all the successful insertions came to maturity on the ninth day. The insertions made subsequent to this date were ineffectual. He also found (9*b*) that in cases in which vaccination was performed on supernumerary fingers which were removed on the fifth day, vaccination performed in the usual way a month later hurried through its cycle, as happens in the revaccination of individuals in whom immunity has not been completely secured.

(ii.) Retardation of the pocks may be brought about by the converse of such conditions, the evolution of vesicles being delayed for ten, fifteen, or possibly even thirty days (37*a*); and some cases have occurred in which vesicles which seemed to have aborted entirely were excited to activity by a revaccination a week or more after the first insertions.

(iii.) The recrudescence of a pock and its breaking down after an interval of some weeks has been noted in cases of invaccinated syphilis (p. 616), and should at any rate excite suspicion as to the purity of the lymph. No allusion is here made to those cases of ulceration of pocks which not infrequently result from some mechanical injury to the scabs.

(iv.) The non-development or abortion of pocks at the points of vaccination probably depends largely on the quality of the lymph and the experience of the vaccinator. The "insertion-success" of skilled vaccinators is very large, amounting to 97-98 per cent.

e. Variations in involution.—As has been observed above, a hard and fast line cannot always be drawn between the local manifestations which result from vaccination in a normal case, and those which so far exceed what is necessary or desirable, as to constitute a source of danger to the individual vaccinated. As regards the vesicles it will be found, that besides those departures from the normal which have been indicated above, many of which may be considered as of little consequence, complications such as severe inflammation round the pocks, ulceration, coalescence of several pocks into one large ulcer, and even local necrosis of the tissues in the region of the pocks, may occasionally occur. Abnormal results in vaccination depend on so many factors—the lymph, the method of vaccination, the treatment of the vesicles, the condition of the individual vaccinated, both previous and subsequent to the operation—that it may be by no means easy in a given case to trace their origin, to detect the cause, or to predict their occurrence; such results may however be expected to follow the careless treatment and injury of the vesicles, the vaccination of feeble or sickly children, lack of care, and unsuitable feeding of children during the vaccination period, or the use of lymph which has been improperly stored, or collected from vesicles with obvious inflammation about them. A further cause of danger possibly lies in the vaccination of children who have recently been exposed to, or who are incubating, some acute disease, such as scarlet fever or measles. This enumeration might be prolonged, but these examples will serve to show that a large number of the inflammatory complications which follow vaccination are directly traceable to some extraneous cause, and cannot in any way be considered merely as variations in the involution of the normal vaccine pock. The cases of suppuration, ulceration, and gangrene are, however, of so much importance that they will be considered under the heading of Vaccinal Injuries (p. 585).

f. Variations in healing and formation of scar.—Vaccination wounds, under normal conditions, should be well and firmly healed before the end of the third week; but in rare cases they may remain open for many weeks, or in still rarer instances, for months. This delay in healing is often due to easily preventable causes, such as repeated injury to the scabs—by other children, by shields, dirty sleeves, dirty applications—and general want of cleanliness; sometimes it is due to the feeble condition of the child combined with unfavourable surroundings: and, though no doubt in exceptional cases the ulceration is definitely started by vaccination, in most of the instances which have come under my own notice I have found that extraneous conditions are, as a rule, far more to blame for prolonged ulceration than any inherent defect in the lymph or in the method of vaccinating. Such cases of deferred healing are not infrequently mistaken for vaccinal syphilis; and a protracted investigation into a series of such cases, which was made by Dr. Barlow and myself, will be found in App. ix. to Final Report of R.C.V. 1896, pp. 320-329. The means by which a diagnosis may, in most cases, be made with certainty will be found in a later section under the head of Vaccinal Syphilis (p. 616).

Although, as already indicated, the scar left by vaccination conforms, as a rule, to a general type, its appearance may present very considerable variations. There is nothing peculiar to vaccination in these abnormalities; they depend largely on the amount of inflammatory reaction at the seat of inoculation. The changes which are most frequently met with are simple hypertrophy or puckering of the scar, and keloid. None of these conditions indicate that the operation has been unsuccessful; and no certain deduction as to the course of vaccination can be made from them. I have seen a case of keloid, for instance, which followed on vaccination made by subcutaneous punctures in which no true vesicles resulted; and Mr. Hutchinson has recorded a case which followed after protracted ulceration of the pocks (28). There is some ground for supposing that the occurrence of keloid depends on the idiosyncrasy of the person, since there is not only a tendency for the condition to spread beyond the limits of the original scar, but, if removed, it tends to recur (23*a*).

Lupus of the vaccination scars is discussed under Invaccinated Tubercle, p. 622.

General symptoms.—These are commonly unimportant; sometimes a slight rise of temperature is noted about the 3rd day after inoculation: this may be followed by remissions, and the pyrexia, if any occur, reaches its maximum generally before the 8th day. These slight disturbances are often the only evidence of a general diffusion of the virus, although eruptions such as erythema, roseola, or urticaria may accompany even the mildest and most favourable cases of vaccination. These rashes, which may develop early in children who are unusually susceptible[1] to the vaccine virus, may occur within four or five days of inoculation, or they may develop during the period of maturity and subsidence of the pocks; they have no special significance, and, as a rule, are not harmful except in so far as they produce irritation and consequent restlessness. Amongst the more usual complications which occur at or about the period of the full development of the pocks are those which are common in all the acute exanthems: they consist in headache (in adults and in elder children), lassitude, irritability, sleeplessness, disturbances of the digestive system—such as anorexia, vomiting, catarrhal diarrhœa; and possibly, during the onset of the vaccinal fever, rigors may occur in adults and in the revaccinated, and convulsions in infants. In relation to these indications of a general infection in some instances there will be evidence of a corresponding disturbance of the circulatory or respiratory apparatus, as shown by increased rapidity of pulse and respiration, bronchial catarrh, or slight temporary albuminuria.

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[1] The problem is generally thus stated, and although children differ widely in their reaction to all kinds of external stimuli, increased susceptibility to the vaccine virus must in

Fürst (23) calls attention to the fact that an increase occurs in the number of leucocytes in the blood during the vaccination period. This increase takes place about the 3rd day, when the local eruption is first developing; and again when the surrounding inflammation is at its height. The leucocytosis diminishes rapidly with the fall of temperature in the early part of the second week, and appears to be proportional to the severity of the symptoms.

PART II

VACCINAL ERUPTIONS AND COMPLICATIONS

Introduction.—Before taking up the general question of vaccinal injuries, attention may be directed to some of the more usual complications which are met with after vaccination: of these the most obvious are the cutaneous eruptions which, although they frequently accompany and sometimes result directly from the inoculation of vaccine lymph, yet for the most part are not peculiar to vaccination, but are common both in infants and adults, and arise from the most diverse causes.

The fact that eruptions of various kinds follow vaccination is now generally recognised. They are as a rule harmless and of simple well-known forms, such as occur in all persons, especially in the very young, under the influence of irritants of widely different kinds and acting in various ways. The rashes produced by belladonna, potassium iodide, mussels, hydatids, septic infections, and antitoxins are familiar to all of us; many of the vaccinal eruptions, however much they may differ in the strictly pathological sense, are clinically of the same kind, and are probably due to a similar cause. Some of them have obtained a fictitious importance in view of the suggestion that an analogy exists between syphilis and

our present state of knowledge be held only to imply that the effect produced by vaccination is unusually severe, since there is no method available for standardising the strength of any particular lymph: so that one child may receive a much stronger dose than another, and the apparent greater susceptibility of one child over another may possibly mean only that he has received a larger dose of the virus.

vaccinia, on the ground that amongst other symptoms roseolous and other eruptions are common to both. The suggestion is of little value when it is remembered that like eruptions are common after infection by diseases differing as widely as variola and cholera.

From such data as are available it seems probable that these rashes, which are by no means peculiar to, or characteristic of vaccinia, signify only that a generalisation of the virus has taken place as the result of the local inoculation; and, further, it seems reasonable to conjecture that they are excited by some chemical irritant, as distinguished from those which, like erysipelas, are due to micro-organisms.

Vaccinal eruptions are usually characterised by their temporary duration and irregular distribution, and by their concurrence with vaccination; they are often attended with much irritation, considerable general disturbance, and some pyrexia.

All kinds of eruptions occurring after vaccination are not infrequently attributed to it; for instance scabies, acne, or even the rash produced by potassium bromide administered medicinally. A case of the latter kind came under the care of Dr. T. C. Fox.[1] A mother who was suckling her child suffered from epilepsy, for which she was taking large doses of potassium bromide: the infant after vaccination suffered from a plentiful crop of bromide pustules, which disappeared immediately on suppression of the drug.

In making the diagnosis of a vaccinal eruption it is necessary to bear in mind these possibilities of error, which may easily excite unnecessary alarm or suspicion in the minds of those who are responsible for the care of recently vaccinated children.

Classification and Chronology. — Various classifications of these eruptions have been made, of which the most satisfactory are those given by Drs. Malcolm Morris and Crocker, to whose works I am much indebted (42, 11*a*).

CLASSIFICATION OF ERUPTIONS AND OTHER COMPLICATIONS FOLLOWING VACCINATION

Eruptions peculiar to vaccination.

1. Those which may result from the inoculation of uncontaminated vaccine lymph :—
   - (*a*) Multiplication of vaccine vesicles by diffusion through digestive, circulatory, or other systems—generalised vaccinia.
   - (*b*) Multiplication of vaccine vesicles by auto-inoculation.
2. Those probably due to some contamination of the lymph or to some peculiarity on the part of the individual vaccinated—vaccinia gangrenosa; vaccinia hæmorrhagica.

Eruptions not peculiar to vaccination, and which may be excited by the absorption of many kinds of virus; probably due to chemical irritation, not to microbic infection.

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[1] *British Journal of Dermatology*, 1892, vol. ii. p. 287. A drawing of a similar eruption alleged to be vaccinal is given in the report of the Medical Officer of the Local Government Board, 1888, p. 28.

1. Urticaria; Lichen urticatus.
2. Erythema multiforme.
3. Roseolous, papular, vesicular, pustular, bullous eruptions (11, 37).
4. Eruptions resembling those of measles and scarlet fever.

Complications not peculiar to vaccination, which may result from the infection of any wound, and are due to some peculiarity on the part of the individual vaccinated, or to the introduction of some extraneous virus into the wounds at the time of vaccination or subsequently.

1. Probably due to peculiarities of the individual: Eczema; Psoriasis; Pemphigus; Local Gangrene.
2. Probably due to some microbic infection of the wounds: Impetigo contagiosa; Tinea tonsurans; Furunculosis; Glandular abscess; Cellulitis; Erysipelas; Septic infections; Tetanus.
3. Causation doubtful; possibly due to microbic infection: Purpura.

Inoculated diseases.

Syphilis; Lupus? Tuberculosis? Leprosy? Cancer? Epizootic disease?

The dates at which these eruptions or complications may be looked for after vaccination are as follows:

1. During the first three days: Erythema; Urticaria; Vesicular and bullous eruptions; Invaccinated erysipelas.
2. After the third day and until the pock reaches maturity: Urticaria; Lichen urticatus; Erythema multiforme; Accidental erysipelas.
3. About the end of the first week, and generally after the maturation of the pocks: Generalised vaccinia—(*a*) by auto-inoculation, (*b*) by general infection; Impetigo; Accidental erysipelas; Vaccinal ulceration; Glandular abscess; Septic infections; Gangrene.
4. After the involution of the pocks: invaccinated diseases, for example syphilis.

The dates at which the various eruptions or complications of vaccination appear after the operation is a matter of considerable importance, as showing the true nature of those cases in which the suspicion of invaccinated syphilis has been raised; and this is especially important since more than one recent writer has endeavoured to trace analogies between vaccinia and syphilis. Thus Creighton (10) states that "the real affinity of cow-pox is not to small-pox, but to the great pox. . . The vaccinal roseola is not only very like the syphilitic roseola, but it means the same sort of thing."

It may be pointed out that the vaccinal roseola appears within a week of inoculation, syphilitic roseola not, as a rule, for a month; that roseolous and erythematous rashes are common prodroma of small-pox, and occur very frequently after the injection of antitoxins—

diphtheritic and others; and again that the date of their appearance and the absence of any distinctive characteristic are opposed to the deduction that they are in any way allied to syphilis.

There does not seem to be adequate ground for concluding that, with the exception of generalised vaccinia, any of the eruptions enumerated above are peculiar to vaccination, or are an essential part of it. Their occurrence in a small number of cases is undoubted; in some instances they certainly depend on extraneous and therefore removable causes, and in others they depend on peculiarities in the individual which are often unsuspected at the time of operation, and cannot be foreseen.

Nothing would be gained by discussing in detail all the various forms of eruption which may follow vaccination. None of them has any peculiar significance in vaccination; many of them are unimportant, and are only mentioned because they are sometimes a cause of anxiety to those who are unacquainted with their harmless character. The more important eruptions, and some of the more troublesome,—such as eczema, impetigo, herpes,—require further notice; erysipelas, syphilis, tubercle, and leprosy, etc., will be considered later in detail.

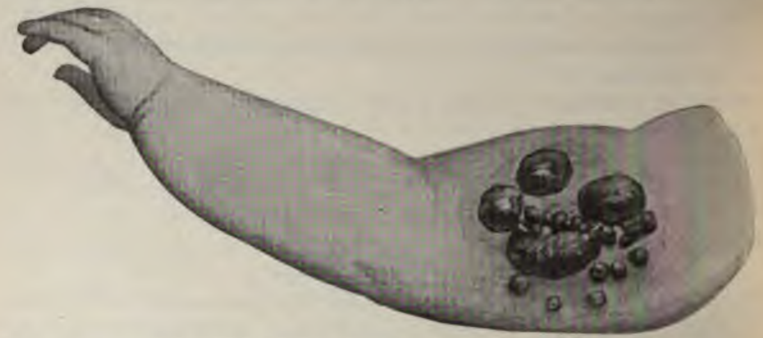

FIG. 4.—Supernumerary vesicles. Stage i. Discrete. Drawing made on 9th day after vaccination with lymph, 46th remove from the calf, and 4th remove from H. T. (*vide* Fig. 8, p. 570). For details, see Case 214, Appendix ix. to Final Report R.C.V., p. 402, No. 500.

From a clinical point of view the eruptions peculiar to vaccination are without doubt the most interesting and important; for if there be any connection between vaccinia and variola, it might be expected that cases would occur from time to time in which the symptoms following vaccination would more closely resemble inoculated variola than the merely local phenomena which are generally associated with vaccination. Such cases do in fact occur; and, though the instances are rare in which vaccination is followed by a general eruption of pocks like those at the point of inoculation, it is (judging from my own experience) by no means very uncommon to find the original insertions surrounded by supernumerary pustules, cf. Figs. 4, 5, 6, so that the appearances closely resemble the drawings of inoculated small-pox by Kirtland, reproduced in the *British Medical*

Journal, vol. i. 1896, p. 1276. I do not intend to maintain that this resemblance implies of necessity any community of nature between variola and vaccinia, possible as this may be for reasons which are discussed by Dr. Copeman (p. 638), but it is certain that, under certain conditions, the course of vaccinia departs from that which is ordinarily observed, and the affection becomes comparable to

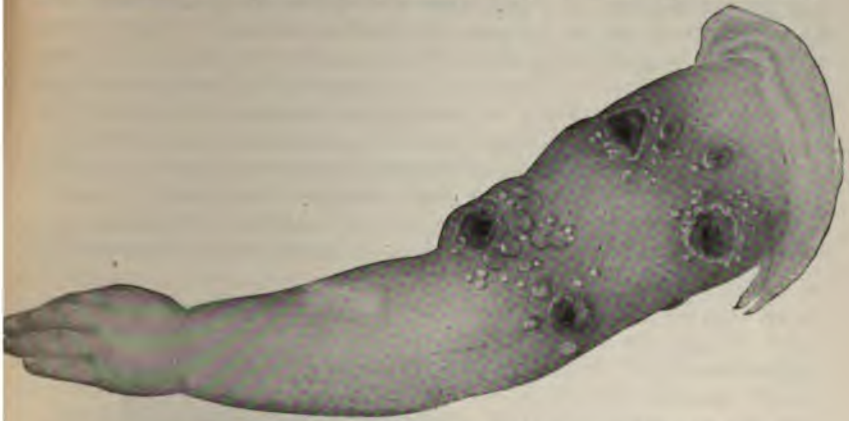

FIG. 5.—Supernumerary vesicles. Stage ii. Semi-confluent. Drawing made on 14th day after vaccination with humanised lymph.

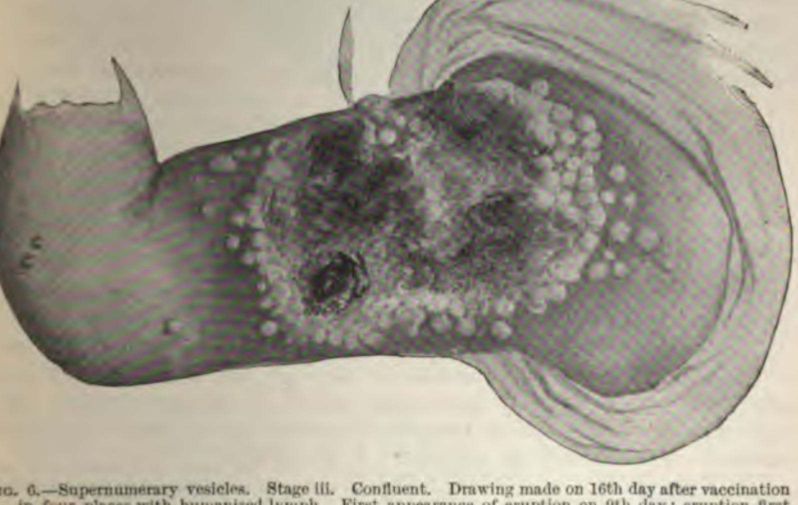

FIG. 6.—Supernumerary vesicles. Stage iii. Confluent. Drawing made on 16th day after vaccination in four places with humanised lymph. First appearance of eruption on 9th day; eruption first confluent on 11th day. Besides the eruption on arm there was only one umbilicated vesicle on abdomen. Compare with Fig. 7, showing inoculated small-pox, and Fig. 8, vaccinia confluent at point of inoculation in a later stage.

one of the exanthems, instead of being characterised only by a local pock without any general eruption. It is also worthy of note that conversely small-pox, by successive re-inoculations of the same individual, may show itself only as a local pock at the point of inoculation without any general eruption (43, 49). This is the case not only in the direct inoculation of variolous lymph, but is equally so in "vaccinations" performed with lymph taken from pocks raised on the calf by the inoculation of small-pox virus. These points of resemblance between variola and vaccinia are of interest whether they indicate any close relationship between the two affections or not; there is little warrant, indeed, for the belief that generalised vaccinia is identical with variola: and, so far as I am aware, no case has been recorded in which vaccinia has

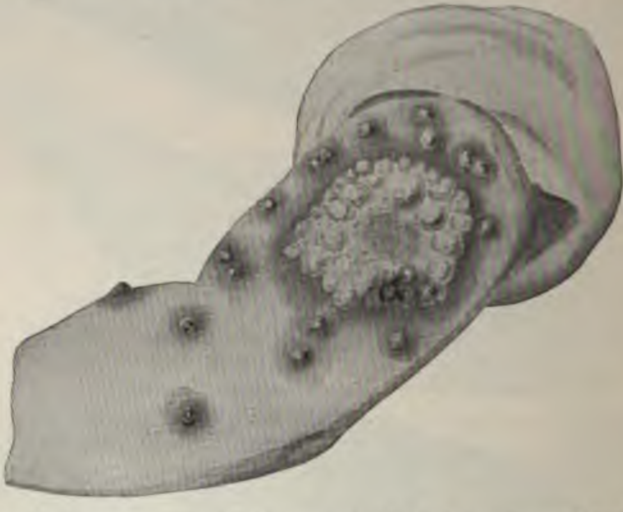

FIG. 7.—Inoculated small-pox. Showing the appearances of a single insertion on the 14th day. From the original drawing by G. Kirtland (1802), lent by Mr. G. W. Collins of Wanstead.

proved to be communicable, except by inoculation, without actual contact with the person infected as is the case in small-pox.

Generalised vaccinia differs in many ways from a general diffusion of vaccine pocks by auto-inoculation through the skin; though both affections indiscriminately have been called by the same name. For convenience of description Longet's classification of these generalised vaccinal eruptions may be adopted. It is as follows:—

1. Spontaneous general vaccinal eruptions or generalised vaccinia—Vaccinal eruptive fever.

2. Vaccinal eruptions generalised by auto-inoculation, for example by scratching—(without any pre-existing lesion of the skin. T. D. A.—Multiplication of pocks by auto-inoculation.

3. To these should be added local vaccinal eruptions (often co

fluent) the occurrence and position of which are determined by some pre-existing cutaneous lesion such as impetigo, eczema, acne, or psoriasis. Some inevitable confusion has been caused by not clearly discriminating between vaccinal eruptions which have occurred on surfaces previously sound, and those in which the seat of the eruption has been determined by some previous local affection.

4. Vaccinal eruptions by migration.

These are too rare to be of any practical importance since they consist of those cases of generalised vaccinia in which the general eruption is the primary manifestation, no local result having followed at the point of inoculation. (Longet, *loc. cit.* p. 205.)

Generalised vaccinia, or vaccinal eruptive fever, occurs, as a rule, comparatively early after vaccination; either one or two days before or one or two days after the pock at the seat of inoculation has arrived at maturity, that is to say, not generally before the 4th day or after the 10th. The date of its appearance may however vary considerably. In Poole's case (App. ix. R.C.V. No. cxciv. p. 70) the eruption began on the 13th or the 14th day (46); in Fox's two cases on the 9th day. The pocks form in successive crops, so that at a given date they may be found in all stages of development; in the three cases alluded to, the eruption continued to appear from the 13th to the 28th day, from the 9th to the 19th, and 9th to the 16th days respectively. When it first appears the eruption is dusky red and rapidly becomes papular, vesicular, and finally pustular; in two or three days the pocks arrive at maturity, and sometimes closely resemble the original vaccine vesicles: in other cases they so much resemble those of variola, that Bousquet declares that there is "so much resemblance between vaccinia and inoculated variola that no physician, however experienced, is in a position to differentiate the vaccinal from the variolous pustule. The most sagacious make mistakes. In a word, at whatever period you select—the 7th, the 10th, the 12th, or 15th day—the characters of the one are the characters of the other. There is no difference between them"[1] (Fig. 7). This is hardly the case, since the eruption of inoculated variola usually appears about the 12th (9th-14th) day. Generalised vaccinia, as a rule, appears earlier (about the 7th day); and the vaccinal fever is generally less pronounced and the constitutional disturbance less marked than in the case of variola. It is not usual for the vaccinal eruption to be found on the mucous membranes or conjunctivæ; but this distinction does not hold good in all cases. Two instances in which the mucous membrane of the mouth was affected, and one in which the vesicles formed on the conjunctivæ, have recently been noted in England. (See L.G.B. Reports, Nos. li. and clxii. App. ix. to Final Report of R.C.V. 1896, pp. 20 and 56.) The similarity of the two affections is such that the suspicion of variola was raised in not a few of the recorded cases before the nature of the eruption was recognised (27, 29, 40*a*, 41, 46).

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[1] An interesting case is reported by Dr. Sharkey (52), "A case in proof of the non-identity of variola and varicella." In this instance, a boy who may have been exposed to the contagion of small-pox (though this is not certain) was admitted to St. Thomas's Hospital suffering from varicella. He was vaccinated, and eight days afterwards an eruption believed to be small-pox began to make its appearance. If generalised vaccinia can be determined by a cutaneous eruption, it is conceivable that this was in fact a case of that disease; and in this connection attention may be called to a remark of Dr. W. T. Simpson, whose researches into the relation of variola and vaccinia are well known (53):—"Vaccine and chicken-pox have always seemed to me to be two elements of small-pox which have become separated in some unknown way; the vaccine retaining the peculiar qualities which affect the body in such a manner as to render it immune from a second attack, while chicken-pox has none of these qualities."

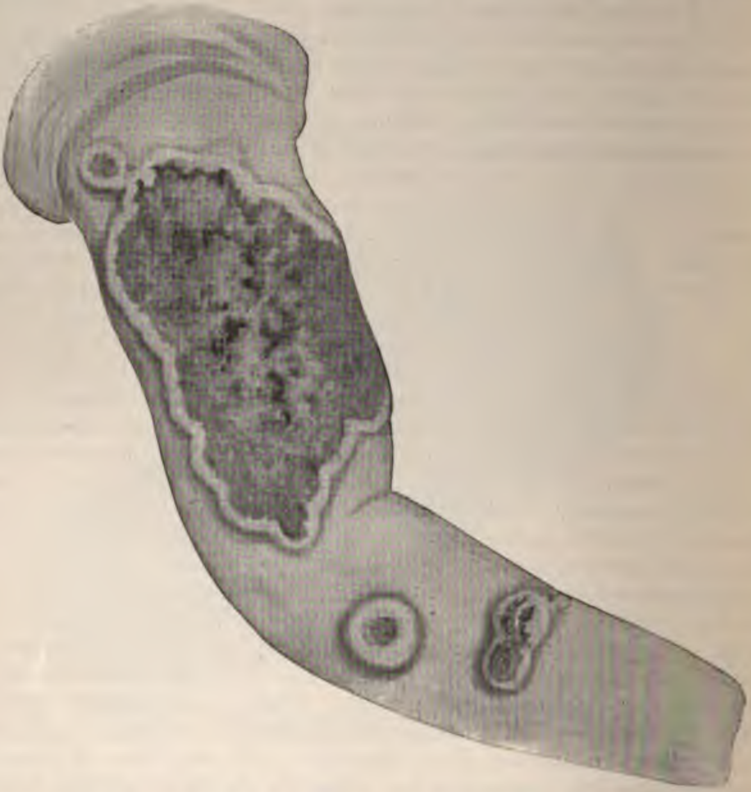

FIG. 8.—Vaccinia confluent at point of inoculation, showing the ulcerated surface left after removal of the scabs. There are two supernumerary pocks on forearm. The drawing was made 43 days after vaccination. For details of case see p. 577; also Case 214, Appendix ix. to Final Report R.C.V., p. 402. Figs. 9 and 10 are from the same case.

The following table, founded on that given by Dauchez, gives the chief points of difference between variola, inoculated variola, and generalised vaccinia—eruptive vaccinal fever:

Day.	Variola (33).	Inoculated Variola (57, 34).	Vaccinal eruptive Fever (Generalised Vaccinia).
1.	Contagion.	Inoculation.	Vaccination.
3.	Period of incubation.	Papule at point of insertion becoming vesicular: vesicle prominent, slightly umbilicated.	Papule at point of insertion becoming vesicular. Supernumerary vesicles form between 3rd and 9th days.
7.	,,	The local pock fully developed by the 7th day.[1]	7th-8th day slight pyrexia.
9. 10. 11.	Malaise, rigors, pain in back, vomiting, reddening and enlargement of glands.	Inflammatory areolæ 10-15 pustules form round points of inoculation; headache, vomiting, pain in back, slight fever.	Maximum of development of pustules, which gradually decrease until the 16th or 17th day.
12.	...	Between the 11th and 13th days the specific eruption of variola appears generally discrete and resembles varioloid.	
13.	Erythematous or roseolous eruptions followed by specific papular eruption on face, wrists, flexor surfaces of arms, etc.	...	The extent of febrile reaction seems to depend on the extent and nature (discrete or confluent) of the eruption, as well as on unessential complications such as ulceration of pocks, excessive local reaction, etc.
15.	Remission of fever.	...	Besnier considers that there is no pyrexia unless there be some complication, for example, glandular enlargement.
17.	Papules become vesicular and umbilicated.	...	Subsidence of eruption generally complete before 21st day.
20 to 22.	Eruption becoming pustular. Secondary fever.		
	The exanthem is contagious.	The exanthem is contagious.	The exanthem is only communicable by direct inoculation of one individual from another.

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[1] The local eruption of inoculated variola is not complete until the 7th day, according to Rayer (47); the general eruption developing from this date, but not being complete until the 13th or 14th day.

The only decisive test whether an eruption following vaccination be a true "vaccinide" or not, is that lymph taken from one of the vesicles at a distance from the original point of inoculation shall be capable of reproducing the specific effects of vaccination in an animal, or in another child (19). That this can be done has been shown by Richard and by Martin. In the former case 15 children were successfully vaccinated; and in Martin's case a heifer was successfully vaccinated from pocks which developed in a child suffering from a general eruption, resulting, as it would appear, from its being suckled by its mother during the period of her vaccination. An interesting demonstration of the true nature of the supernumerary pocks was given in a case of vaccinia generalised by auto-inoculation, reported by myself (1), in which the child suffering from pocks on its lips and face inoculated its mother's breast; the subsequent vesicle showed no departure from the ordinary appearances or evolution of a vaccine pock.

Causation of generalised vaccinia.—Apart from any peculiarity of the lymph, and without assuming abnormal receptivity on the part of the individual, the eruption of vaccination may cease to be purely local if the virus is administered, not through the skin, but by the digestive, circulatory, or respiratory systems; and also (apart from auto-inoculation, which is considered later) if during the vaccination period there is some coexistent, general cutaneous eruption, such as sudamina.

A generalised vaccinial eruption has been produced in children who had sucked their vaccination pocks;[1] and it has been determined in those who had previously proved insusceptible to vaccination, by the intentional administration of powdered vaccine crusts (7). Similarly, as has been noted, a general vaccinal exanthem has appeared in a child suckled by its mother whilst undergoing vaccination (41).

It is of interest in connection with this case to note that children whose mothers have been successfully revaccinated previous to their confinements have been vaccinated after birth without result; showing, possibly, that the effect of the mother's vaccination was shared by the fœtus in utero. In investigating this point a large number of observations have been made; the most remarkable of which are those of Burckhardt and Kellock on women, and those of Rickert on sheep. Burckhardt vaccinated 28 pregnant women, and subsequently vaccinated 6 of the children whose mothers had been successfully vaccinated. The operation was unsuccessful in all of them. Kellock (35) vaccinated 36 women in various stages of pregnancy, and found (*a*) that the infants resisted vaccinatio directly as the stage of pregnancy at which the mother was vaccinated and (*b*) that the fœtus seemed to be more readily affected in the mult parous than in those of a first pregnancy. His results were as follows:—Of 14 children of primiparas, vaccination was successfull performed on the infant in every case in which the mother had bee vaccinated earlier than the 7th month of pregnancy; whilst the operatio failed in 5 of the infants whose mothers had been vaccinated later tha the 7th month. In the case of the children of the multiparous, n less than 16 proved insusceptible to vaccination, even though in some

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[1] Étienne; quoted by Longet.

e experiments of Straus, Chambon, and Menard (55) have a
on this point. They found that the blood serum of a calf,
fore the pocks were healed, produced immunity in other animals
ame species when infused into the venous system. Chauveau
demonstrated that a generalisation, manifested by an eruption
f reproducing the ordinary results of vaccination, could be excited
tion of horses through the digestive, circulatory, and respiratory
as well as by injection into the subcutaneous tissue (8).

e observations, which are in agreement with the clinical
ove that the results of vaccination may be obtained without
uction of the local pock: and under given conditions the diffusion
rus is occasionally demonstrated by the appearance of a cutaneous
similar to that which occurs in the acute exanthems, even if it
tirely analogous to them.

inia generalised by auto-inoculation.—Allied to spontaneous
sed vaccinia are those sequels of vaccination which are caused
more or less wide distribution of vaccinal pocks by auto-
ion. These supernumerary pocks may be caused by scratching
e-nails after they have been in contact with the vaccine pocks;
ccidental contamination of surfaces denuded of epithelium by
h cause as eczema or impetigo: they may be produced in any
he body accidentally brought into contact with virus from the
vesicles. Such cases are common, and references may be
them in the papers already referred to, especially Dauchez,
and Poole: drawings of remarkable cases are given in my paper
linical Society's *Transactions*, 1893, ii. p. 114, pl. ii., and in
paper, "Drei Fälle von generalisierter vaccine," Munchen, 1893.
nber of pocks varies from one or two upwards; and in the cases
the eruption has become confluent the number is often very
The majority of these cases are unimportant, and result only

occur in the most unexpected ways, as, for instance, in the case of a man who, having chafed himself in riding, applied some vaseline to the sore place out of the same pot which his wife had used for the arm of their child who had been recently vaccinated: the result was a large crop of vaccine vesicles on the buttocks. If vesicles occur on the eyelids, or the eyeball, the consequences may be serious; this latter accident, however, is of great rarity. In five cases recorded by Berry the ulceration was confined to the eyelid. The symptoms vary with the seat of the initial lesion and the condition of the patient as regards immunity against vaccinal inoculation (21, 26, 56). Thus infection of a

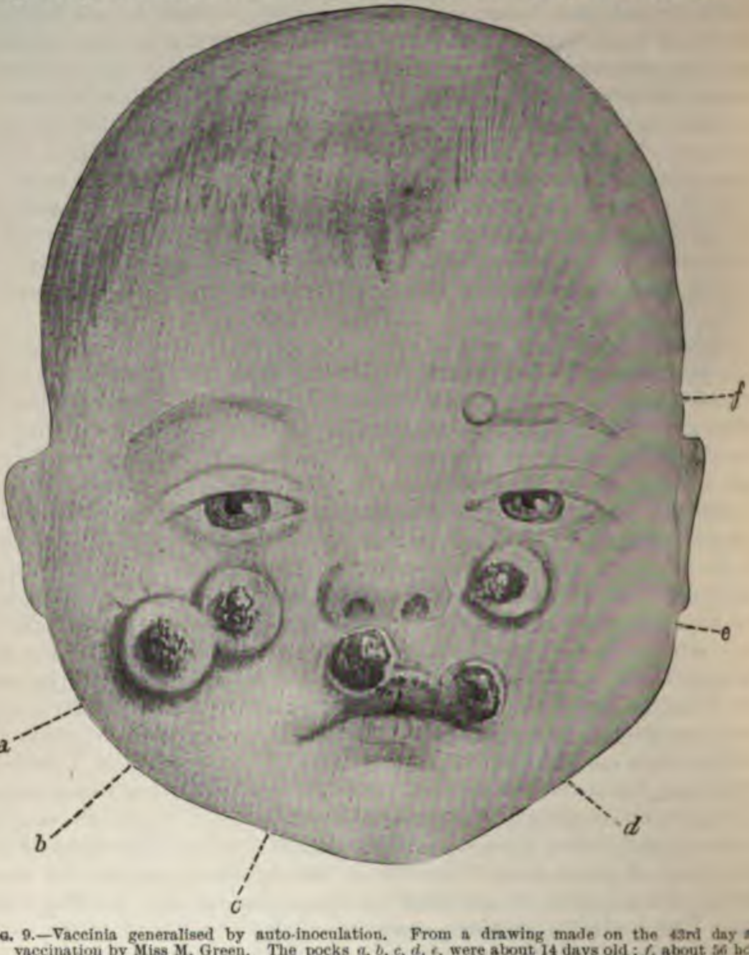
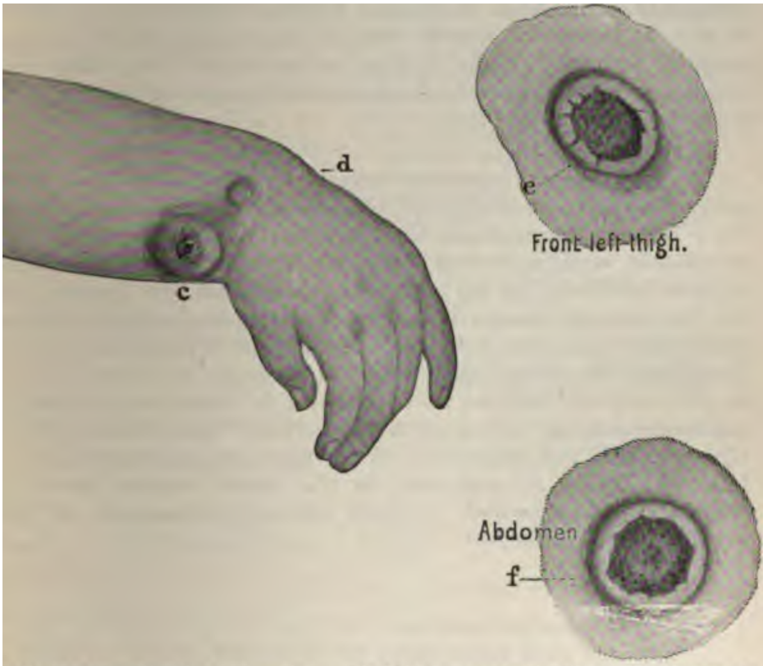


Fig. 9.—Vaccinia generalised by auto-inoculation. From a drawing made on the 43rd day after vaccination by Miss M. Green. The pocks *a*, *b*, *c*, *d*, *e*, were about 14 days old; *f*, about 56 hours. *Lymph*, humanised; 42nd remove from calf. *Eruption* round points of inoculation confluent on 14th day. See Fig. 8. *Pocks* continued to appear until the sixth week after vaccination. Mother's breast was inoculated, and the pock ran a normal course. For reference to details of case, see p. 511.



—Vaccinia generalised by auto-inoculation. Pocks from various parts of the body. *c* measured ut ½ in. transversely; *e*, ¼ in.; and *f*, ⅜ in. The drawings were made on the 43rd day after cination: *c* was then about 12 days old, and *e* and *f* about 14; *d*, about 48 hours. There was le inflammatory thickening round them; no true induration. In the centre of *e* and *f* there a clean granulating surface. Cf. Figs. 8, 9, pp. 570, 574.

l Normal College for the Blind, Upper Norwood—in which institu- if in any, such cases would probably be found—resulted in the

One other form of accidental auto-inoculation calls for special notice, since mistakes in diagnosis might occasion much unnecessary distress. Cases have been recorded (M. Morin and Behrend (16)) in which sores have been produced around the anus, and on the mucous membrane of the vulva, by the accidental transference with the fingers of pus from the vaccinated arm. It is hardly necessary to point out that such sores, especially if macerated by the contact of the parts and ulcerated, might be looked upon as venereal (as in the instances referred to) if due care were not exercised. A knowledge of the possibility of such an occurrence and the history of the case ought to prevent this error, even if (owing to the position of the sore, and the stage of evolution of the original vaccine vesicle from which the infectious material was derived) the characteristic appearances of the vaccine pock should have been lost.

A definite case of confluent vaccinia, in which the eruption became generalised by auto-inoculation and possibly also by absorption of the virus through the digestive tract, has been recorded by myself (1). In this case it would seem that the abnormal conditions were primarily due to some peculiarity on the part of the child, since the lymph used was the forty-second remove from the calf; and three other children were successfully vaccinated from this child without complication of any kind. The lymph was traced backwards and forwards for three generations, in all twenty-five children were examined in immediate relation to this particular case, the only abnormality detected being that in four out of eight children vaccinated with lymph from the same source, no result followed; whilst in one child, in the fourth remove, twelve supernumerary pocks appeared. A brief chronological summary of the case is given for reference :—

H. J. K., æt. three months; Vaccinated with humanised lymph, 42nd remove from calf. Generalised Vaccinia; Death (Figs. 8, 9, 10).

First week . .	9th November 1892	Vaccination with humanised lymph, forty-second remove from calf. (Of eight vaccinations by three vaccinators with lymph from same source, four were unsuccessful, but without complication or abnormal result.)
Second week . .	16th November 1892	Inspection. Four healthy vesicles, to all appearances normal.
Third week . .	23rd November 1892	The four pocks coalesced into one, and became covered with dark brownish green scab. Innumerable secondary pocks, at first vesicular, formed round points of inoculation, cf. Fig. 6, p. 567.
Fourth week . .	30th November 1892	Secondary eruption pustular; a large pock appeared on back of head, which eventually scabbed and dried up. (Pocks appeared on face, arms, legs, abdomen, and thighs.)
Fifth week . .	7th December 1892	The supernumerary pocks at points of insertion confluent; eventually a large open sore formed.
Sixth week . .	14th December 1892	No improvement in child's condition.
	17th December 1892	Pulv. hyd. c. creta, gr. ½ given three times a day with some improvement. Pock formed above inner angle of left orbit.
Seventh week .	21st December 1892	Vesicle forming behind right ear; this aborted within 24 hours.
	25th December 1892	Child's condition worse. Mother's breast became inoculated from suckling the child. Pock ran a normal course. Mother had not been revaccinated.
Eighth week . .	27th December 1892	Death.

There is no evidence to show that such cases are due to any particular strain of lymph, whether humanised or taken direct from the calf (51, 31); they are of great rarity, and must be regarded as accidental complications rather than as essential elements of vaccination.

Such a case as that narrated above opens out the whole question of vaccinal immunity, which it would be impossible to discuss at any length in this place. If the observations of Cory, Trousseau, Mognier, Dumont-Pallier, Damaschino, Besnier, and others are conclusive and final, there is evidence to show that under ordinary circumstances the receptivity of an individual to successive vaccinations in series gradually diminishes during the second week, and usually becomes extinct before the fourth.

Cory (9*a*) found that when vaccinations were performed in series by a single insertion on each of eleven successive days, those made after the ninth day were unsuccessful, and he concluded that immunity was attained at this period. It is certain that during the first week after vaccination an individual may be readily revaccinated or may contract small-pox; for it does not appear that any considerable degree of immunity is established until after the pocks have reached maturity. Immunity probably reaches its maximum about the fourth week after vaccination; but the standard of resistance varies with each individual, and probably also with the dose and activity of the virus. In the case given above, pocks continued to form for thirty days certainly, and probably longer; so that no rule can be made universally applicable. Vaccinia generalised by auto-inoculation may, however, be expected to occur, if at all, before the third week after vaccination.

Great variations may be met with in susceptibility to vaccinia as well as to small-pox, or any of the acute exanthems. It is commonly recognised that one attack of small-pox renders the individual more or less immune against contracting the disease again; and similarly that one successful vaccination protects, at any rate for a time, against the probability of a second successful inoculation. But it would seem that in some persons one attack is no safeguard against a second. This is well illustrated by a case which came under the notice of Dr. Clifford Allbutt, in which a woman had small-pox three times, and was also three times successfully vaccinated. Such a case seems to set at defiance all laws deduced from ordinary observation, and may be regarded as the exception which proves the rule. The following table gives a brief outline of the facts:—

1858.—A. B.; born ——. Mother developed small-pox when infant was eight days old, and child had it in a mild form.
" When three months old successfully vaccinated (three scars).
1881.—Successfully revaccinated (two scars).
1883.—Mild attack of small-pox.
1892.—(September). Successfully revaccinated (two scars).
" (November). Unsuccessfully vaccinated.
1893.—Unsuccessfully vaccinated.
1896.—Very mild attack of small-pox; (but indubitable, T. C. A.)

There is strong evidence that this persistent falling away from immunity in this respect existed in other members of this patient's family.

Vaccinia hæmorrhagica.—Besides the cases in which the sequence of events and the appearance of the eruption are analogous to those found in the acute exanthems, there are others in which the pathological position is at present doubtful: in these cases vaccination is followed by an eruption which is more or less "hæmorrhagic." The eruption may vary in intensity, from the faintest petechiæ to general hæmorrhage; and may be characterised by a few scattered petechiæ, subcutaneous ecchymoses, or severe hæmorrhage from mucous membranes, such as hæmaturia. Such cases are extremely rare; and, although there is no direct proof of it, they are probably analogous to the well-known cases of hæmorrhagic small-pox and scarlet fever.[1] They are too few in number to warrant any opinion as to their causation; but, apart from any peculiarity in the lymph, it might be expected that such complications would occasionally arise in scorbutic, rachitic, and cachectic children; the cause which determines the nature of the eruption being rather the condition of the child than any abnormality of the lymph.

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[1] See 3 cases recorded by Dr. Gregory, Bergeron and Barthelemy, Dauchez, *l.c.* pp. 137-139.

Vaccinia gangrenosa.[1]—A disease closely allied to generalised vaccinia, if not a modification of it, has been described by Hutchinson (29), Stokes (54), Crocker (11), and others, under the name of vaccinia gangrenosa. It is to be regretted that this name has been used for another affection of quite a different character; namely, local gangrene or necrosis at the points of vaccination (46*a*). Vaccinia gangrenosa is an acute exanthem occurring at the end of the first or the early part of the second week after vaccination. The eruption begins in the form of discrete papules with an inflamed base, which ulcerate and scab over, pus forming under and round the scab, while the ulceration extends both in depth and laterally. In this way a central black slough is formed, which after its removal leaves an irregular, unhealthy ulcer, often with overhanging edges. The ulcers may be single or confluent. In Crocker's case, from which the above description is taken, the largest ulcers were ¾ in. in diameter and ⅓ in. in depth.[2] Hutchinson observes that the diagnosis of these cases lies between variola, varicella, and vaccinia; and Crocker includes in his account of the disease a fourth affection, "dermatitis gangrenosa," independent of any one of those named, and probably due, as he believes, to some pathogenetic organism—possibly bacillus pyocyaneus. It is not yet possible to state the precise relationships of these cases, but it seems certain that the eruption can be determined by vaccination, and probable that the disease is a true exanthem, possibly allied to variola or varicella; but there is no evidence to decide whether it be due to a mixed infection, or is the direct result of a specific virus acting upon an individual whose tissues are altered by syphilis, tubercle, rickets, or other constitutional malady, all of which have been considered as favouring its production.

Eczema.—Vaccination is performed, in the majority of cases, at a period of life when eczema and other inflammations of the skin are extremely common; and it is no wonder that the operation is sometimes followed by an acute outbreak of such disorders. I have not met with any case in which it seemed probable that the affection was transmitted by the operation; and in many cases which have come under my own observation, and which have been recorded by others, the acute attack following vaccination or injury to the scab is merely a recrudescence of a pre-existing condition; or is an expression of a family tendency. Out of a total of 394 cases of alleged vaccinal injury which have more or less directly come under my own notice during the last eight years, thirty, or about 7·5 per cent, were cases of non-specific skin eruptions;[1] and there does not seem to be any reason to suppose that vaccination is the specific cause of any large number of severe cases of eczema.

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[1] For illustrations see Mr. Hutchinson's paper (29) and Crocker's *Atlas of Diseases of the Skin*, pl. xli. fig. 1.

[2] Mr. Hutchinson refers (*loc. cit.* p. 5) to models 206 and 209 in the Guy's Hospital Museum, which he believes to be taken from cases of varicella gangrenosa. He also gives references to other cases besides his own. See also *Archives of Surgery*, vol. iii. 1892, plate xvlii.

The statistics of 600 cases of eczema which had been under the care of Dr. T. C. Fox show that 249 (41·5 per cent) came under treatment before the end of the first year; and in forty of these cases eczema is known to have occurred before vaccination. Of 161 cases in which the date of onset is recorded the eruption commenced in eighty before the end of the third month, and in sixty-nine during the next three months. This seems to give *prima facie* ground for supposing that vaccination is not responsible for any considerable increase in the number of cases; which is the conclusion drawn by Dr. Fox. At the same time it must be noted that there is a definite rise in the numbers in the fourth and in the ninth months, the periods at which the irritation of vaccination and of teething respectively, might be expected to come into play. The actual numbers are as follows:—

0-1 month	33	6-7 months	10
1-2 months	22	7-8 ,,	4
2-3 ,,	25	8-9 ,,	23
3-4 ,,	39	9-10 ,,	1
4-5 ,,	23	10-11 ,,	1
5-6 ,,	7	11-12 ,,	3

In some instances an eczema which has been intensified by vaccination subsequently improves; but as a rule a pre-existing eczema is made distinctly worse by vaccination, and not only is it undesirable to vaccinate an eczematous child on account of the risk of aggravating the affection, but also because there is danger of causing a generalised vaccinal eruption on the affected parts.

Impetigo or Porrigo.[2]—The occurrence of this contagious affection of the skin after vaccination is little to be wondered at when the conditions under which the children of the poor have to live are taken into consideration. Under any circumstances pus is readily inoculated from one individual to another, so that local superficial sores are produced; and when such a source of contagion is introduced into a household where the inmates are dirty, ill-fed, and overcrowded, it is obvious that ample opportunity is afforded for the spread of a purulent affection both from and to a vaccinated child. I have seen cases of impetigo which have originated from injury to the vesicles by dirty sleeves, dirty shields, dirty night-clothes, by exposure to infection from purulent discharges in other children, by scratching the vaccination wounds and inoculating distant parts of the body with the finger-nails. A case, reported to the Commission as one of vaccinal injury, may be mentioned, exemplifying the lack of attention to cleanliness which is often the main factor in bringing about these kinds of skin eruption, in which I found a child wearing a hat the lining of which was soaked with pus from an impetigo which had occurred a year previously.

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[1] See Case 25, App. ix. R.C.V. 1896, p. 241, and Case 98, p. 273, and Cases 95, 102, 127, etc.

[2] For plates, see *Atlas of Diseases of the Skin*, New Sydenham Society, fasciculus x. pl. xxviii., and *Atlas of the Diseases of the Skin*, by H. Radcliffe Crocker, fasciculus x. pl. xxxix. and xli. Cf. also Cases 24, 82, 129, 196, App. ix. R.C.V.

It is unnecessary to discuss this question at length: it cannot be doubted that impetigo may follow any wound, vaccinal or other, in which pus is formed; and that the liability to the affection is enormously increased by want of cleanliness and bad hygienic surroundings. It is a more serious question whether these disorders are ever actually communicated by vaccination. If impetigo is due, as is probable, to the presence of pyogenic cocci in the discharges, it is possible that some lack of care in the selection of the vaccinifer might lead to the inoculation of one child from another. I have only investigated one case in which there was any evidence that such communication might have occurred; and in this instance the vaccinifer did not begin to suffer from impetigo until some days after the lymph had been taken from his arm, so that there was no proof that the child was capable of communicating the disease at the time that he was used as a vaccinifer. It is also possible that both vaccinifer and sub-vaccinee may have suffered from the subsequent eruption in consequence of accidental contamination of the vaccination wounds by the lancet used for the operation.[1]

In foreign countries groups of cases of impetigo have followed vaccination in such a manner as to leave little or no doubt that the affection was communicated by the operation.[2] The lesson to be learned from these cases is obvious; namely, that there is risk in using any individual suffering from a communicable disease as a source of lymph.

Herpes tonsurans.—The accidental inoculation of the tricophyton tonsurans in the process of vaccination has been observed abroad (Hagar (25), Eichstadt (21)), but I am not aware that any case has occurred in England. Like many other communicable skin diseases, it is common in poor and ill-cared-for children; and it is not surprising that in rare instances vaccination should be the means by which it is transmitted from one child to another.

In the case of an affection of the skin so readily communicable from one child to another as tinea tonsurans, it may be fallacious to conclude that the disease was transferred in the act rather than at the time of vaccination; since to undress a number of children in a hot, crowded waiting-room, such as that in which vaccination is sometimes performed, must facilitate the distribution of the spores, and render infection more than usually easy.

Pemphigus; Psoriasis. — The occurrence of these affections after vaccination has been recorded (Dauchez (17), Rioblanc (50)); but if any connection exist between the operation and the eruption it is as yet undetermined. If it should be proved eventually that these diseases result from the inoculation of specific cocci or saprophytes, it may perhaps be shown that in rare instances they are communicated by vaccination; but up to the present time no sufficient evidence has been brought forward to show that this is probable. It is certain that in some cases the individual vaccinated was predisposed to and had suffered previously from skin eruptions similar to those which appeared subsequently; and in others that the child vaccinated was in a cachectic condition as the result of some affection, which had lain dormant until roused into activity by the constitutional disturbance of vaccination.

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[1] See Case 180, App. ix. R.C.V. p. 366.

[2] See Fürst, *loc. cit.* p. 72, and Third Report R.C.V. 1890, p. 135, and Peiper, *loc. cit.* p. 64.

The influence of the exanthems on the course of vaccination is not easy to determine. It is certain that such chronic or subacute affections as eczema, impetigo, and possibly psoriasis, are not uncommon causes of generalised vaccinia (*q.v.* p. 573); but whether the acute specific fevers—such as scarlet fever, measles, and varicella—can determine and precipitate a general cutaneous vaccinal eruption is a question which, for lack of sufficient data, cannot as yet be definitely stated.

The difficulty of arriving at any precise knowledge on these points is greatly increased by the fact that the nature, extent, and variety of post-vaccinal eruptions have hitherto received inadequate recognition; so that cases of generalised vaccinia have been regarded as variola, and cases of erythematous, vesicular, or papular eruptions, as scarlet fever, chicken-pox, or measles.

It is probably rare for vaccination to be complicated by any one of the acute specific fevers; and still more rare, should this happen, for any abnormality to occur. In isolated cases it is often a matter of great difficulty to decide whether an erythematous rash is scarlet fever, or a vesicular rash varicella. Cases have come under my own notice, as well as under that of others, in which there were grounds for supposing that errors of diagnosis had been made; as, for instance, cases in which a simple vaccinal eruption had been regarded as evidence of invaccinated syphilis.

It would not be unreasonable to suppose that the course of a vaccination performed during the incubation period of scarlet fever or measles might be disturbed, and that the tissues at the point of inoculation might undergo necrosis similar to that which occurs in noma or cancrum oris; but even if such cases do occur, they are so rare that we are compelled to regard them as accidental complications which are inevitable in all conditions of life, and of pathological interest rather than of clinical importance. Dr. Hopwood, for many years resident at the London Fever Hospital, informs me that he has himself vaccinated a considerable number of persons in all stages of scarlet fever, and has seen many vaccinated by others under similar circumstances, without any evil result. He has also seen persons vaccinated shortly before an attack of scarlet fever, and yet in them no serious complications. In estimating the importance of facts observed by the resident medical officer of a well-equipped hospital, it must be borne in mind that vaccination wounds are much more likely to pursue a normal course in the cleanly conditions of an hospital, than in the crowded and often filthy surroundings in which many children are compelled to live; and that given a case of vaccination, complicated by scarlet fever, in some miserably poor home, it will be well-nigh impossible to decide with certainty which of the many unfavourable conditions had been mainly instrumental in bringing about any abnormal result which may occur.

There is reason to believe, however, that under favourable conditions normal vaccinia can run parallel with scarlet fever, varicella, and even with variola, if the latter be contracted before immunity is secured.

The influence of congenital syphilis on vaccination.—The statement has not infrequently been made that it is difficult or even impossible to obtain a normal vaccine vesicle in a child who is suffering from congenital syphilis.[1] This certainly is not the case. If the child be not cachectic, vaccination may pursue a normal course, and the vesicles may be good, giving no indication whatever of the danger of collecting lymph from them for further vaccinations. This fact is of the utmost importance in the selection of a vaccinifer. The diagnosis of congenital syphilis must be made from an examination of the child, and a knowledge of its family history; and no reliance whatever should be placed on the appearance of the vaccinated arm. If the vaccinated child be cachectic there is a danger that vaccination may be followed by ulceration or sloughing at the point of inoculation; or that some one of those complications may arise which occur in feeble children, who have little or no power of resistance against local inflammation.

The influence of vaccination on latent disease.—Symptoms of scrofula,[2] tuberculosis,[3] congenital syphilis,[4] sometimes occur after vaccination; and the lesions, without adequate ground, are apt to be attributed directly to vaccination. It is in accordance with ordinary clinical observation that disease, hitherto quiescent, should be lighted into activity by some factor which is not specifically concerned in its causation. Thus a mechanical injury, an acute specific fever, prolonged anxiety, or insufficient food, are often followed by pulmonary or meningeal tubercle, or by some other local manifestation of tuberculosis.

Primary vaccinations are frequently performed at or about the period when symptoms of congenital syphilis may be expected to declare themselves; and cases have come under my observation in which children known to have been previously suffering from congenital syphilis have been vaccinated, and in whom the subsequent evidences of syphilis have been put down to vaccination.[4] In a particular instance it may not be easy to prove that a lesion which follows vaccination is not directly the result of the operation; but in most instances the history of the case, if fully inquired into, will give conclusive evidence as to the real origin of the malady.

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[1] *British Medical Journal*, 1880, vol. i. p. 191.

[2] Cases No. 131, p. 307, and No. 187, p. 374, Appendix ix. R.C.V. 1896.

[3] Case 187, p. 374.

[4] Cases No. 227, p. 413; No. 309, p. 438; and cf. Cases 198, p. 386; 202, p. 389; and 326, p. 447, *loc. cit.*

REFERENCES TO PARTS I. AND II.

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PART III

VACCINAL INJURIES. ALLEGED AND REAL.

Introduction.—The practice of vaccination has been opposed on three grounds:—(i.) *Theoretical.* It is said that vaccinia and variola are totally distinct diseases, and that the inoculation of cow-pox does not therefore exercise any specific protective power against small-pox (3). (ii.) *Statistical.* It is stated that so-called cow-pox is nothing else than human variola artificially transmitted; and that statistics of small-pox epidemics demonstrate not only that vaccination does not protect against small-pox, but that it actually causes it.[1] (iii.) *Practical.* It is alleged that the injuries caused by vaccination are so numerous, and so terrible, that there is no justification for the continuance of a practice which may be powerless for good (29*a*).

This is not the place to discuss the first two propositions, which, if both were true, would be mutually destructive. The third proposition, namely that which relates to the extent and severity of vaccinal injuries, is one which deserves the most careful study. It is alleged that syphilis, tubercle, and other diseases, such as cancer and lupus, have been inoculated at the time of vaccination; and that pyæmia, erysipelas, and various other inflammatory affections result directly from the operation of vaccination as it is at present performed. Syphilis and tubercle have not infrequently been inoculated in the rite of circumcision (20*a*, 24*a*), in tattooing (13*b*), and in other purely accidental ways (13*a*, 24*b*). It might therefore seem probable, on *a priori* grounds, that in the practice of vaccination there is real danger to be apprehended from these sources. The purpose of the following pages is to inquire how far these allegations are borne out by fact; and, if admitted to be substantially correct, to endeavour to ascertain in what proportion of cases injury has been found to occur.

The influence of vaccination on general infantile mortality is discussed in the Final Report of the Royal Commission on Vaccination, paragraphs 377 and 378, p. 105; the following passage epitomises the present state of knowledge on the subject:—

"Without encumbering our report with the details relating to pyæmia, bronchitis, diarrhœa, and skin diseases, which are all said to have increased owing to the mischievous influence of vaccination, we may confidently say that there is no evidence to justify the statement. It is, however, worth while pointing out, that comparing as before the period 1883-87 with the period 1863-67, the increase of deaths under one year of age from diarrhœa and dysentery in Leicester was 4·2 per cent, whereas in England and Wales it was 0·5 per cent. A similar comparison in respect of bronchitis shows the increase in Leicester to be 112·8 per cent, in England and Wales 73·3 per cent. It seems clear that as regards general infantile mortality Leicester has not gained by its avoidance of vaccination. Whilst in England and Wales the mortality of children under one year of age had between the periods selected for comparison decreased 7·5 per cent, in Leicester the decrease was only 2·8 per cent. Upon the whole, then, we think that the evidence is overwhelming to show that in the case of some of the diseases referred to, vaccination cannot have produced any effect upon the mortality from them, and that it has not in the case of any one of them increased the mortality to a substantial, we might even say an appreciable extent."

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[1] Vogt, Prof. Adolf (Bern), *Memorial concerning the Effect of Vaccination*, etc., chap. ii. p. 692, "Identity of Variola Vaccina and Variola Vera," chap. viii. p. 707, "Variola Epidemics produced by Vaccine Inoculation." Paper forwarded to the Royal Commission on Vaccination. Appendix to Sixth Report R.C.V. p. 689 *et seq.*

That harm occasionally results from vaccination in individual cases cannot be doubted; but whether the number of cases in which injury is inflicted be large or small, it is interesting to note that the annual infantile death-rate has not increased since vaccination was made compulsory; it has, in fact, diminished. (See Final Report R.C.V. p. 102, para. 385.) The actual numbers are—1838-42, 152 per thousand births; 1847-50, 154; 1851-60, 154; 1861-70, 154; 1871-80, 149; 1881-90, 142.

It is obvious that these figures give no certain data for determining the actual number of deaths which result directly or indirectly from vaccination; neither does the diminution in the annual death-rate show that no deaths result from the operation; but they indicate that no appreciable increase in the death-rate, whether due to vaccination or not, has occurred. There are also other data available for forming a reasonably accurate estimate of the facts.

Statistics of deaths and injuries.—The number of deaths or of serious injuries which result annually from vaccination may be arrived at with considerable certainty. From the Registrar-General's returns it appears that in the years 1881-89 the number of deaths certified as connected with vaccination was 476, or nearly 53 a year. During these nine years 6,739,902 primary vaccinations were performed. This gives an average of 1 death to 14,159 primary vaccinations. During the three years from 1st November 1888 to 30th November 1891, 205 alleged cases of injury were inquired into by the medical department of the Local Government Board; and from 1st June 1889 to 1st July 1896, 421 additional cases were investigated by the Royal Commission on Vaccination. Of the cases inquired into by the Local Government Board, Dr. Coupland and I came to the conclusion that in approximately 20 per cent the influence of vaccination was doubtful. Of the cases investigated for the Commission by Dr. Barlow and myself, about 16 per cent were probably altogether unconnected with vaccination; while of the cases inquired into by Dr. Luff, nearly 40 per cent are placed by him in the same category.

As these figures are and can only be taken as an approximation to the actual facts, it is probable that no serious error will be made in supposing that, of the total 626 cases investigated, some 20 per cent may be set aside as unconnected with vaccination; leaving 495 cases of death or vaccinal injury which have been adequately inquired into during the last eight years: this gives an annual average of 61·3, or a slightly larger number than that which is arrived at from the Registrar-General's returns, which refer to cases only in which death has occurred.

From these statements it will be seen that, however valuable to the community at large, vaccination is not exempt from that liability to accident which exists in all human affairs. Operations even of a trivial kind sometimes prove fatal; and that most beneficent means of alleviating pain which has been universally adopted—the administration of anæsthetics—is not unattended by risk, and occasionally results in death. The percentage number of deaths which occur annually in England from chloroform is far greater than that which results from vaccination. It is, in fact, nearly seven times as great; and though the risk from ether is much less, the percentage number of deaths per annum traceable directly or indirectly to anæsthetics is appreciably greater than that which follows vaccination,[1] while the total number is approximately the same. It cannot be argued that the rare fatalities attendant upon vaccination which occur are sufficient ground for rejecting the practice if it can be proved to be beneficial on the whole. If the practice of vaccination is to be discredited, it must be by showing that the injury thereby inflicted on individuals is out of all proportion to the good which is gained by the community; and not by exaggerating, distorting, and multiplying every isolated instance of injury which occurs. The following pages have been written with the object of stating fairly what is the amount and kind of injury inflicted by vaccination as at present practised; how much of it is inevitable, how much preventable, and by pointing out the dangers, to show incidentally how many of the risks may be avoided.

In this, as in other branches of pathology, it is incumbent on the medical profession to impose on itself, as a condition of assenting to any doctrine, the obligation of setting forth conscientiously all that can be said against it, no less than all that can be said in its favour.

Erysipelas.—*Relative importance of inflammatory complications.*—Among the complications of vaccination, those are most to be dreaded which are common to all wounds. The most grave are erysipelas, cellulitis, ulceration, abscess, and septicæmia. None of these are peculiar to vaccination; they constitute the dangers of any local lesion of the skin; and, considering the age of the children vaccinated, the conditions under which thousands of them live, and the treatment to which in defiance of the most elementary principles of cleanliness the wounds are often subjected, it is surprising that, as investigation proves, so few cases of serious injury occur.

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[1] I am indebted to Dr. Childs, secretary of the Anæsthetics Committee, Brit. Med. Association, and to Mr. G. Rowell of Guy's Hospital, for the actual figures, which are as follows:—Deaths from anæsthetics recorded: 1891, 46; 1892, 41; 1893, 46; 1894, 66; 1895, 61; 1896, 8½ months, 48. The deaths from chloroform are roughly 1 in 2000, and from ether 1 in 20,000.

The relative importance of these inflammatory complications may be gathered from the fact that of 205 cases investigated by the Local Government Board,[1] and 189 cases investigated by Dr. Barlow and myself (11) (all of which have been fully inquired into, and as far as possible placed under definite headings),[2] 133 and 94 respectively come under the category of "inflammatory."[3] In other words, of 394 cases of alleged vaccinal injury recorded during the years 1888-1895 with which I have had directly or indirectly to deal, no less than 57·6 per cent resulted from one or other of the specific forms of inflammation. The percentage is, indeed, considerably higher than this; since many of the cases in which the suspicion of invaccinated syphilis has been raised, proved on investigation to be cases of vaccinal ulceration, or some other such lesion; and might properly, therefore, have been included in the inflammatory class. Thus, approximately, 60 per cent of all cases of vaccinal injury in this country are probably due to some form of inflammation; erysipelas being the most important and of the most frequent occurrence.

To form some estimate of the frequency of post-vaccinal erysipelas recourse may be had to the statistical and clinical facts which were laid before the Vaccination Commission (18). It will be seen from the returns of the Registrar-General for Scotland, that during the years (1855 - 1863) immediately preceding the Act for making vaccination compulsory in Scotland, 28·36 per cent of all deaths from erysipelas occurred during the first six months, and 5·02 per cent in the second six months of life; and that during the years (1864-1887) which immediately followed the passing of the Act, the numbers were 28·88 and 5·35 per cent respectively. This shows conclusively that no new cause, resulting in a different distribution of mortality from erysipelas, came into play in consequence of the passing of the Vaccination Act. Again, the Leicester statistics show that, comparing the years 1883-1887 (at which time vaccination had largely fallen into abeyance) with the years 1863-67, the infant mortality from erysipelas, which in England and Wales had decreased 16·7 per cent, in Leicester had increased 41·5 per cent. The comparison here made is between Leicester and the whole of England and Wales, a comparison not perhaps strictly exact; but the figures are remarkable, and warrant the conclusion that the neglect of vaccination in Leicester did not at any rate lessen the number of deaths from erysipelas amongst the infant population.

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[1] An analysis prepared by Dr. Sydney Coupland and Dr. T. D. Acland of the Reports made by Inspectors of the Local Government Board, Appendix ix. to Final Report R.C.V. 1896 (1).

[2] These figures do not give the total number of cases investigated by the medical officers of the Commission, but refer only to those reported on by Dr. Barlow and myself.

[3] For classification adopted, see Appendix ix. *loc. cit.* p. 2.

Erysipelas may be defined, according to present knowledge, as an acute specific inflammation of the skin caused by definite micro-organisms, and characterised (i.) by a tendency to spread, mostly by continuity; and (ii.) by a general intoxication running parallel with the local inflammation.

It has been suggested, without adequate proof, that erysipelas following vaccination is "a stage in the evolution of cow-pox"—"a throwing back to one of the original characters of that communicable infection" (14); and that it is "the prime note of vaccination" (31). These hypotheses were anticipated by Bohn, when some twenty years ago he wrote that "the clear, pure lymph of a true Jennerian vesicle possesses the power of engendering erysipelas" (12). It does not admit of doubt that these statements, made in the first two instances with the object of bringing the practice of vaccination into disrepute, are not founded[1] upon any more secure basis than that erysipelas sometimes starts from the vaccination vesicles, as it may start from any wound.

It is possible that the virus of erysipelas may be, and sometimes though rarely is, introduced with vaccination; but no proof has been brought forward to show that the vaccine lymph commonly contains this virus, or that erysipelas is a necessary or essential part of vaccination.

Pfeiffer, Crookshank, Landmann (23), Kitasato, Sternberg, Copeman, and others have demonstrated (*a*) that vaccine lymph may contain organisms capable of producing erysipelas; but they have also shown that, so far as present knowledge goes, none of these organisms is the specific organism of cow-pox: and (*b*) that vaccine lymph which has been deprived of all known[2] living pyogenetic organisms, still produces the characteristic effects of vaccination (26). It follows from this that complications which result from the presence of streptococcus pyogenes aureus, erysipelatosus, and other pathogenetic organisms, are, so far as can at present be stated, accidental, and in no way an integral part of the process of vaccination.

Landmann (24) has shown that lymph which contains no known pathogenetic and but few saprophytic organisms, gives unusually good results when used for vaccination. In forty persons vaccinated with such lymph the areola in no case exceeded $\frac{3}{8}$ inch in breadth; and Kitasato's (21) experiments have led him to the conclusion that the inflammatory symptoms which not infrequently follow vaccination are mainly if not entirely due to the presence of extraneous pathogenetic organisms in the lymph.

These researches prove—

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[1] It is not of any practical importance whether Jenner thought that the inflammation excited by the cow-pox was "erysipelatous" or not. There is no necessity for limiting the pathological knowledge of to-day by statements made nearly 100 years ago (1799). See *Further Observations on the Variolæ Vaccinæ*, by Edward Jenner. Reprinted by E. Crookshank, 1889, p. 187.

[2] As stated in the introduction, p. 557, there is some ground for believing that vaccinia is caused by a specific contagium, as it is not capable of cultivation on ordinary media. (Klein and Copeman.)

(i.) That the virus of erysipelas is entirely distinct from the virus of vaccinia, and has no necessary pathological connection with it.

(ii.) That it is possible to prepare vaccine lymph which is entirely free from those pathogenetic organisms which are known to excite the specific forms of inflammation.

(iii.) That vaccine lymph freed from all living pyogenetic or saprophytic organisms has not lost thereby its power of producing characteristic vaccine vesicles.[1]

(iv.) That lymph containing the streptoccocus of erysipelas may, if the dose be sufficient, excite erysipelas starting from the point of inoculation.

The incubation period of erysipelas.—Much evidence has been adduced from cases in which the initial lesion was known, to show that this period may be as short as two hours, and possibly in exceptional cases as long as eight days. Thus in thirty-one out of thirty-six cases recorded by Tillmanns it was three days or less; and in a large majority of cases it was less than sixty hours.

The length of the incubation period of post-vaccinal erysipelas seems to correspond with Tillmanns' observations; since, in many cases in which there has been evidence to show that the lymph was at fault, the erysipelas began at an early period after vaccination; that is, within the limits of time which experimental or accidental inoculation has shown to be the probable incubation period of the disease: and it may be stated generally that the sooner after vaccination erysipelas occurs, the more likely it is to have been invaccinated. In a great majority of cases post-vaccinal erysipelas begins during the second week after the operation, at a time when the normal incubation period of erysipelas is probably long passed, and when, pus being formed at the point of vaccination, there is a ready "nidus" for the reception of any of those wound infections which so frequently follow mechanical injuries resulting in a breach of surface.

Whether erysipelas inoculated at the time of vaccination can remain dormant for days or weeks is a question to which at present no definite answer can be given. Some of the coincidences which have come under my notice are remarkable. For instance, eleven children were vaccinated on the same day (2); in one case only two pocks formed, and on the eighth day the child was revaccinated from one of his co-vaccinees, in two places. Both these children, who lived many miles apart, and as far as I could ascertain never met again, and were not attended by the same doctor, sickened with erysipelas within twenty-four hours of one another about the twenty-sixth day after vaccination, and died within four days of one another, thirty-nine and forty days after vaccination respectively. In another case the vaccinator, apparently ill at the time, died of erysipelas four days after inspecting a child's arm which was inflamed. The child died four days later, also of erysipelas.

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[1] Fürst concludes that the vaccine virus is contained in the living cellular elements, and that no form of bacterium has yet been cultivated outside the body capable of producing definite vaccine pocks. (*Loc. cit.* p. 9, *q.v.* for a summary of the various opinions on this matter.)

In 1891 I undertook a series of experiments on calves and rabbits, with the object of determining (if possible) whether, were the virus of erysipelas inoculated simultaneously with vaccine lymph, the disease might remain in abeyance until the formation of the pustule on the eighth or ninth day. It is conceivable that with a weak virus in a strongly "refractory" individual the appearance of erysipelas might be delayed until the resistance of the tissues had been overcome by the formation of pus at the point of inoculation; and that a dose of the virus, which under ordinary circumstances would have been inoperative, might then give rise to symptoms after the normal incubation period (about three days) of erysipelas had passed. These experiments did not, however, solve the problem completely; the conditions were necessarily so different from those of vaccination that any deductions made from them would require rigorous criticism.

In the numerous cases of post-vaccinal inflammation which I have investigated I have found that, as a rule, when erysipelas occurred more than three or four days after vaccination, it was impossible to obtain adequate proof that it had been invaccinated; or proof that it was due to the condition of the instruments used, or to some act on the part of the vaccinator at the time when the operation was performed.

Cases of vaccinal erysipelas.—In the following cases of vaccinal erysipelas there is sufficient evidence for concluding that the lymph or method of vaccination was the actual cause of the disease.

1. Two children were vaccinated with lymph stored in tubes; both of these children died with symptoms of general diffuse inflammation of the skin which spread over the entire body. In the first child the inflammation was well marked by the third day; in the second child the first vaccination failed entirely, but it was revaccinated from the same source: "soon" after the second vaccination the arm became red and swollen, and by the fourth day the inflammation had spread to the elbow. The tube from which this revaccination was made, and another of the same batch, were examined by Dr. Klein with the following results:—

(*a*) The former showed the presence of numerous colonies of the streptococcus of erysipelas.

(*b*) The latter yielded cultures of staphylococcus pyogenes albus liquescens.

These cases support the belief that lymph, contaminated with specific organisms in sufficient quantity, may be expected to show the results of the inoculation of such organisms, whether vaccination be successful or not; and may give rise to local symptoms within a few hours of inoculation, before the vaccine vesicle has had time to arrive at maturity: that is to say, the course of the erysipelas in all probability will not be delayed by the vaccination, but will be the same as if inoculation with the micro-organism had taken place apart from the vaccination (3).

2. Five children were vaccinated from the same source (4); in four of these erysipelas subsequently appeared, and one died. The

vaccinifer sickened with erysipelas ten days after lymph had been taken from its arm. The cases are noteworthy for several reasons:—

(*a*) It will be seen from the following table that the severity of the symptoms varied inversely as the length of the incubation period.

(*b*) All the sub-vaccinees of the vaccinifer (who himself subsequently suffered from erysipelas) did not suffer from erysipelas; one escaped entirely; the others suffered in varying degrees, and the initial symptoms appeared at varying intervals after inoculation.

These gradations in the severity of symptoms, and length of incubation period, are in harmony with what is known of such factors as dosage, virulence, and receptivity, which determine the effect produced by any given virus.

CASE No. 115.

TABLE showing date of appearance of erysipelas, etc., in a vaccinifer and four sub-vaccinees.

No. in Register.	First appearance of Erysipelas after Vaccination.	Severity.	Course.	Result.
Vaccinifer— No. 157, A. S.	17 days	Slight.	Subacute.	Recovery.
Sub-Vaccinees—No. 166, M. H.	6 hours	Great diffuse swelling; abscesses.	Acute.	Death on 20th day.
Do. No. 163, B. S.	16 hours	Great diffuse swelling; pyæmia.	Subacute.	Abscesses on scalp, scapula, shoulder joints, wrists, etc.; not fatal.
Do. No. 164, F. H.	5 days	Less severe; no suppuration.	Subacute.	Recovery.
Do. No. 165, T. W.	19 days	Less severe; axillary abscess after 5 weeks.	Chronic.	Recovery.
Do. No. 167, T. C.	None	...	...	Vaccination normal. Six children successfully vaccinated from this case.

3. In another series of cases there was ground for believing that some infective material had been introduced with the vaccine lymph. Sixteen children were vaccinated: in four of them septic symptoms appeared within 12 hours; in four within 36 hours; in three within 60 hours;

in two before the fourth day; in one before the eighth day. Of one there is no record (5).[1]

The following table is of interest as showing the dates after vaccination at which erysipelas appeared in 100 cases which have been adequately investigated. Of these, ninety-six were inquired into and reported upon by the medical staff of the Local Government Board; the remaining four, added to complete the hundred, were investigated by myself (6). It shows that the great majority of cases occurred at a date after vaccination outside the limits of what is believed to be the normal incubation period of erysipelas. Only nine cases occurred in the first three days, while no less than ninety-one appeared during the subsequent weeks.

No deduction must be made from this table as to the relative frequency of erysipelas after vaccination with the various kinds of lymph; since it is impossible to ascertain the total number of vaccinations performed in England with lymph derived from each of the several sources named during the period to which reference is made.

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[1] The details of these cases, which were inquired into by Dr. Barlow and Dr. T. H. Thompson, will be found in Appendix ix. Final Report R.C.V. p. 229; the reports are of such length as to prohibit their introduction here, even in abstract.

[TABLE

TABLE showing date of appearance in 100 cases of post-vaccinal erysipelas occurring between November 1888 and February 1892.

	Erysipelas occurring in						Vesicles known to have bee opened.
	No. of Cases.	First Week.	Second Week.	Third Week.	Fourth Week.	Fifth Week.	
HUMANISED LYMPH							
1. Arm to arm	48	First day 3 Fifth day 3 Sixth day 2 Seventh day 4	23	10	1	2	15
2. Tubes	18	Sixth day 1 Seventh day 1	8	7	0	1	3
3. Tubes N.V.E.	1	...	1				
4. Points N.V.E.	3	Third day 1	2	...	...	...	2
5. Method of preserving not stated	6	Second day 1 Fifth day 1	3	1	...	...	1
CALF LYMPH							
1. N.V.E. direct from calf	2	...	2	...	...	...	1
2 Other sources—tubes	6	Second day 1 Sixth day 2	3	...	...	...	1
3. N.V.E. points	1	...	1				
4. Conserve--source not stated	1	...	1	...	...	...	1
5. Source and method of preserving doubtful	2	Sixth day 1	1				
SOURCE OF ORIGIN NOT STATED	12	Second day 3 Fourth day 1 Seventh day 4	4				
Totals	100	29	49	18	1	3	24

The history of the nine cases in which erysipelas supervened in the first three days is important. In two instances pathogenetic organisms were found in tubes of lymph from the same source as that which had been used to vaccinate the children.[1] In five cases there was strong evidence for believing that the lymph was at fault; since more than one child out of each of the three groups of vaccinees (vaccinated on the same day) to which these children belonged suffered from erysipelas; and in each instance the vaccinifer suffered from superficial inflammation of the arm. In one case a child was vaccinated with a tube of lymph which had been opened a week previously; another was vaccinated when three weeks old, in an infirmary, the bedding on which the mother and child slept having been in a ward in which a case of erysipelas had occurred: the ward had, however, been "fumigated" with sulphur. Thus in all these cases of early post-vaccinal erysipelas, except possibly the last, there were circumstances which make it probable that the erysipelas was due to some extraneous cause which came into play at or about the time of vaccination.

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[1] Cf. Cases of vaccinal erysipelas, p. 591.

Such cases might be multiplied; but enough has been said to show that symptoms may be expected early in those instances in which there is ground for believing that erysipelas, or some septic infection, was introduced at the time of the operation: and, further, that the symptoms may vary greatly in intensity.

It seems probable, if one only of a number of children vaccinated from the same source develop erysipelas later than the fourth or fifth day, that the erysipelas is due to some extraneous cause, and is not invaccinated. On the other hand, if a number of children vaccinated from a common source develop erysipelas before the fourth day, only one or two of the whole batch escaping, the probability is very great that the erysipelas is directly due to the lymph or to some factor introduced at the time of vaccination.

Erysipelas starting from vaccination wounds may be communicated to other persons, as is proved by the records of some of the foundling institutions; notably those of Vienna and St. Petersburg. In the former no less than 31·47 per cent of the deaths were due to erysipelas.[1] Nor is this to be wondered at: the children were vaccinated indiscriminately, the weakly with the strong, often when they were but seven or eight days old. The lymph was collected by the attendants; the vaccine pocks were plastered with zinc powder, until stinking pus exuded from below the scabs (13), and the daily bath was forbidden. Allusion is made to these cases since they have been instanced by a recent writer to show that "the erysipelas engendered in the process of vaccinal infection, or, in other words, by *exaggeration of the normal areola* and infiltration, may become the source of erysipelatous contagion to others, just as erysipelas of other origins may so become" (15). That erysipelas following vaccination may be communicated to other persons is beyond doubt; but this fact does not prove that erysipelas is an integral part of vaccination, although it is certain that it frequently follows vaccination when simple and well-known principles of hygiene are disregarded. In the Foundling Hospital at St. Petersburg, after the adoption of such ordinary rules of cleanliness as are essential to the well-being of all infants, especially of the feeble or the very young, the number of cases of erysipelas was reduced by two-thirds.

No attempt has been made hitherto to show that the areola which forms round healthy vesicles can actually communicate erysipelas to others; or that it contains micro-organisms which are capable of exciting the specific forms of inflammation (16). Even if it be capable of proof that the areola is caused by extraneous pathogenetic bacteria, and not solely by the irritation of the developing pustule, no evidence has yet been adduced to show that these organisms play any essential part in the process of vaccination.

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[1] In Würtemburg, during the same time, only one case of post-vaccinal erysipelas was ascertained to have occurred amongst 500,000 children living under ordinary conditions (Fürst, *loc. cit.* p. 69).

From Tillmanns' experiments, and from clinical observation, it would appear certain that erysipelas need not necessarily start from the point of infection (9). This latter point is of interest as bearing upon the question whether the areola be "erysipelatous." It is certain that erysipelas may occur before the areola is formed, as well as after it has subsided; that it may involve the areola, and subside, leaving the areola still round the vesicles; and that it may occur in a distant part of the body while the areola is still present.

Sources of danger independent of the lymph.—Apart from any intrinsic qualities in the lymph, and independent of all sources of danger from the methods employed in its collection and storage, there are elements of extraneous and often readily avoidable risk in the circumstances of the infant, and in the method in which the operation is at times performed. The use, in one case, of a mechanical scarifier which it was practically impossible to clean, and, in another, of ivory points which had frequently been recharged, may be instanced.

Hypotheses concerning the nature of vaccinal erysipelas which do not take these and such causes into account are likely to be fallacious. The facts are that erysipelas is common in infants, especially as a result of open wounds; and that vaccination acts as nothing more than an exciting cause, not infrequently providing the starting-point.

Vaccinal ulceration and glandular abscess.—Of the other inflammatory complications which may follow vaccination, those of the most frequent occurrence are ulceration at the point of inoculation, and glandular abscess. Nearly 4 per cent of the vaccinal injuries inquired into by the Local Government Board (1888-1891) were due to one or other of these lesions; and in all the cases some extraneous cause was found which might have determined the departure from the normal. An enumeration of some of the many local applications which I have known to be made to the vaccine pocks, and which may well be regarded as the origin of ulceration or suppuration, will be found on p. 614. Disaster on a large scale, in times now long past, has been courted[1] by using as a source of lymph "The shirt sleeve of a patient stiff with purulent discharge from a foul ulcer,"—"Matter found in great plenty on the sleeves of children's shirts,"—"Lymph in one instance taken from vesicles on the ninth day; the vaccinifer, three months old and suffering from twelve pocks, being carried from village to village and used to vaccinate 104 children." This list might be extended, but such examples sufficiently show the ignorance of some persons who have undertaken to perform vaccination; the results —"deep-seated ulcerations and violent inflammations"—being such as might be expected from such disregard of the most elementary laws of hygiene and cleanliness.

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[1] Creighton, *The Natural History of Cow-Pox*, pp. 115-118, *q.v.* for references to the original documents.

I have seen several cases in which ulceration of the pocks, glandular abscesses, erysipelas, and even septic intoxications followed the vaccination (7) of infants whose conditions of life were unfavourable. Amongst these are included illegitimate children born in destitution, and, it may be, vaccinated when a few days old, in a workhouse infirmary: from the comparative comfort of which they are removed before the vaccinated arm is well, to surroundings which could not fail to be harmful even to a healthy child. It is not to be wondered at that such infants, ill clothed and worse fed, a burden to their mothers, and sometimes with their lives insured, should succumb to an operation even so trivial as vaccination. No mention would be made of such cases here were it not that they have frequently been made the subject of legal inquiry, and the child's death attributed to vaccination. In the majority of cases in which inflammatory complications follow vaccination there are numerous factors which tend to bring about the catastrophe; and it is illogical to draw any definite conclusions as to the origin of the lesion without giving full weight to the extraneous influences which, apart from vaccination, may have been brought to bear upon the individual case. Under the heading Syphilis, p. 616, will be found tables giving the points of difference between vaccinal ulceration and syphilitic chancre; but it may briefly be said here that, as a rule, vaccinal ulceration is well marked at a time when syphilitic chancre would not yet have developed; and that vaccinal eruptions, if present, differ widely from those which occur as secondary phenomena in acquired syphilis (cf. p. 617). Their development is irregular, their distribution unsymmetrical, they are often intensely irritating, and they tend to conform to the various forms of erythema and urticaria rather than to the papular, squamous, and macular eruptions of secondary syphilis.

Gangrene at the point of vaccination.—In isolated cases gangrene occurs at the point of vaccination, and it sometimes follows vaccination in syphilitic subjects. One such case is reported by Balzer; one by Wheaton. I have myself investigated two cases (8), in one of which the syphilitic parentage is certain and in the other probable. It is not unreasonable to suppose, if the individual vaccinated be the subject of inherited disease, and the operation be performed when the child is very young, that the result is largely due to the condition of the tissues, and not necessarily to any abnormal quality of the lymph. Three cases have been recorded and summarised by Mr. Hutchinson (20) in which there was no known exciting cause for the local lesion except the fact that the child had been vaccinated: it is probable that none of these children was syphilitic, and it is possible the phenomena may have been the result of idiosyncrasy in reference to the vaccine virus. Mr. Hutchison instances, in support of this view, the occurrence of noma and cancrum oris, forms of spreading gangrene which have nothing to do with syphilis, but which may occur as sequels of the acute specific fevers, such as measles or scarlet fever.

Such cases have not infrequently been mistaken for syphilis, and in making the diagnosis it is necessary to bear in mind the natural history and evolution of that disorder. The differential diagnosis will be found on p. 616.

Tetanus[1] may follow as an accidental infection of any wound; as a complication of vaccination it is of the utmost rarity. I am only acquainted with one case of tetanus in more than five million vaccinations in this country (cf. Case x., App. ix. R.C.V. p. 6), and in none of the recorded cases is there any evidence that the tetanus was invaccinated. It has been known to follow vaccination in South Africa in a series of adult natives, who immediately after being vaccinated worked under a tropical sun. Such cases as the latter require no comment; they only show that ordinary caution is necessary even in so slight an operation as vaccination.

Other wound infections, such as *osteomyelitis* (36) and *icterus* (!) (32), are stated to have followed vaccination, nor is this surprising considering the vast number of vaccinated children living in every degree of dirt, destitution, and misery. None of these have come under my own observation; and, so far as I am aware, no cases have occurred in the United Kingdom during the last ten years. So far as the practice of vaccination is concerned they are of no importance; for they only emphasise the fact, which needs no demonstration, that any wound may become septic if the conditions are unfavourable; and that, given an infected wound, the results will depend primarily on the nature of the contamination, and, in a less degree, on the peculiarities of the individual.

Septic infection in relation to various kinds of lymph.—There are no accurate data for determining whether erysipelas and the "septic infections" are more common after the use of calf lymph, or humanised lymph; or of lymph stored in tubes, on points, or as a conserve.

It has been thought that the use of "calf lymph" might afford some increased security against these inflammatory complications; and this supposition seemed to be corroborated by the fact that diffuse inflammation round the pocks in calves is rarely observed. No case has been recorded at the Lamb's Conduit Establishment; Voigt in 1888 had seen one case only amongst 2500 calves; in conjunction with Dr. Carl Menge,[2] I have found that calves are singularly refractory to inoculations of the streptococci of erysipelas, even in association with vaccinia. Our observations are corroborated by Klein (22).

In my own experiments no diffuse inflammation was produced in calves by inoculation (after linear scarification of the skin) with (*a*) streptococci cultivated direct from a case of acute facial erysipelas; (*b*) virulent cultures direct from Prof. Fraenkel of. Königsberg; (*c*) culture from the same source five months old; (*d*) serum from the blisters in a case of acute facial erysipelas; (*e*) cultures of micrococcus pyogenes aureus and albus from a virulent case of cellulitis. In the latter case the vaccination, which was performed simultaneously, pursued a normal course. Culture (*a*), when injected subcutaneously into the ear of a rabbit, produced inflammation within thirty-six hours, and suppuration in less than sixty hours. These experiments are not complete; but they are in accordance with the observed facts that superficial wounds, such as those caused by vaccination, do not so readily become the starting-point of erysipelas or cellulitis in the calf as in man; and that a virulent culture sufficient to cause abscesses in one species of animal may not produce any evident result in another. Again, these facts are in agreement with the well-known axiom that the effect of any contagion depends not only on the dose and the virulence of the poison, but also on the susceptibility of the individual inoculated.

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[1] *Archives of Dermatology*, 1880, p. 188, contains a reference to a case recorded by Ross, *Southern Clinic*, 1879, vol. i. p. 468. Toms, *Medical News*, 1894, vol. lxiv. p. 209, *q.v.* for reference to five other cases; symptoms of tetanus did not supervene in any of the reported cases within three weeks of vaccination, six out of the seven cases have proved fatal.

[2] Unpublished observations by Carl Menge, M.D., Strasburg, and T. D. Acland, M.D., Aug. 1891.

Reliance must not, however, be placed on the comparative insusceptibility of the calf to erysipelas and septic infections through superficial wounds, to secure the immunity of vaccinated children from erysipelas. Most of the inflammatory sequels of vaccination, if not all, are due to causes which are removable, and therefore, under certain conditions, preventable; the lymph itself rarely contains organisms capable of directly causing erysipelas, and it is probable that all pyogenetic organisms can be removed from lymph, by treating it with glycerine (*vide* p. 652). The result of my own observation leads me to the conclusion that vaccination, as now performed directly from the calf, is, *cæteris paribus*, followed by greater inflammatory reaction than when humanised lymph is used; but, as stated above, there are no trustworthy figures to show the percentage of cases of erysipelas or cellulitis which follow vaccination by either method.

In the earlier days of vaccination, when even serious surgical operations were performed with little regard to cleanliness, and when the causes and prevention of sepsis were not understood, the collection, storage, and use of lymph for vaccination was not carried out with the care necessary to prevent contamination with pyogenetic or pathogenetic organisms. There is good ground for the hope that the researches of Sternberg, Kitasato, Landmann, Copeman, and other pioneers, will lead to improved methods of obtaining and preparing vaccine lymph; and that persons having the care of vaccinated children will learn that many of the so-called results of vaccination may be avoided. It will then be found that the one complication of vaccination most to be feared, comparatively infrequent as it now is, will, except in the rarest instances, be unknown.

The results obtained by Voigt (of Hamburg), whose experience has extended over a period of twenty years, during which time he has performed some quarter of a million vaccinations, may be taken as fairly representing what is possible. His observations are the more important as he has special arrangements for tracing and investigating every case of vaccinal complication. During the last five years, out of 100,000 vaccinations, he has seen one case of axillary abscess; two of abscess (locality not stated); one of furunculosis; two of erysipelas; and five of vaccinal ulceration, with only one death. But it must not be forgotten that to secure such results nothing may be omitted which can help to make the operation aseptic. There are many possibilities of sepsis from the belly of the calf, the opened tube, the recharged point, the mechanical vaccinator which cannot be or is not sterilised, the hands of the operator, and the infant's surroundings. These dangers, if recognised, can often be avoided but cannot be disregarded, even in so simple an operation as vaccination. There is no ground for believing that the septic complications of vaccination are "stages in the evolution of cow-pox," or "throwings back to its original characters"; but there is much evidence to show that the methods at present employed for the production, storage, and use of lymph occasionally fail to reach that perfection of asepsis[1] which is necessary in any surgical operation, however small, and which is especially necessary in the case of very young children.

REFERENCES TO PART III. ON VACCINAL INJURIES

1. *Appendix IX. to Final Report of Royal Commission on Vaccination*, 1896, p. 2—2. *Ibid.* Case 106, p. 277.—3. *Ibid.* Cases xxxi. and lxv., pp. 13, 24.—4. *Ibid.* Case 115, p. 289.—5. *Ibid.* Case 23, pp. 229, 233.—6. *Ibid.* Cases 124, 163, 164, 166.—7. *Ibid.* Cases 113, 118, 207, 309.—8. *Ibid.* Cases 202, p. 389, and 207, p. 395.—9. Ballard. Table R.C.V. Appendix, p. 209.—10. Balzer. *La France médicale*, 1890, quoted by Martin, *New York Medical Record*, 1890, p. 44.—11. T. Barlow and T. D. Acland. *Letter to the Chairman of the Royal Commission on Vaccination*, unpublished.—12. Bohn. *Handbuch der Vaccination*, Leipzig, 1875, p. 174.—13. *Ibid. Pathologie der Vaccine*, Leipzig, 1875, p. 175.—13*a*. Bollinger, Prof. "Ueber die Infectionswege des tuberculosen Giftes," III. Abtheilung für *Allgemeine Pathologie und pathologische Anatomie des X. Internat. Congres zu Berlin*, 1890.—13*b*. Collings, D. W., and Murray, W. "Three Cases of Inoculation of Tuberculosis from Tattooing." *British Medical Journal*, 1st June 1895.—14. Creighton. *The Natural History of Cow-Pox and Vaccinal Syphilis*, Lond. 1887, p. 105.—15. *Ibid. Loc. cit.* p. 105.—16. *Ibid. Loc. cit.* p. 103.—17. Crookshank. Evidence before the R.C.V. Fourth Report, p. 48, Questions 11,058, 11,104, 11,135, and 11,218, etc.—17*a*. Crookshank, E. M. *The History and Pathology of Vaccination*, Lond. 1889, vol. i. p. 464.—18. *Final Report Royal Commission on Vaccination*, 1896, p. 105.—19. Fürst. *Loc. cit.* p. 101.—20. Hutchinson. *Archives of Surgery*, i. pp. 97-116. Cf. also R.C.V. Sixth Report, pp. 216-223.—20*a*. Hutchinson, Jonathan. "On Syphilis conveyed in Circumcision," *Syphilis*, p. 115. Lond. 1889.—21. Kitasato. *Sei-i-kwai:* Medical Journal, Tōkyō, 1896, pp. 91 and 176.—22. Klein. "Observations on the Concurrent Inoculation of different Infections in the same Animal Body," *Report of Medical Officer of Local Government Board*, 1891-1892, pp. 126, 127.—23. Landmann. *Hygienische Rundschau*, 1895, p. 975, and 1896, p. 441.—24. *Ibid. Loc. cit.* p. 976.—24*a*. Peiper, E. *Internationale klinische Rundschau*, 1889, p. 72.—24*b*. *Ibid.* "Zur frage des Uebertragung der Tuberculose durch die Vaccination,"

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[1] The question of bacterium-free vaccine lymph was discussed at the 68th Versamml. Gesellschaft Deutscher Naturforscher und Aertze zu Frankfurt a. M. Sept. 1896. Cf. also Neidhart, *Hygienische Rundschau*, No. 21, 1896, p. 1073, and *Chemiker Zeitung*, Oct. 1896, p. 788.

Internationale klinische Rundschau, 1889, p. 73.—25. PFEIFFER. "Ueber Impfkrankheiten," *Deutsche med. Wochenschrift*, 1892, p. 198.—26. STERNBERG. *Medical Record*, New York, 1896, p. 677.—27. *Ibid.*—28. TILLMANNS. "Erysipelas," *Deutsche Chirurgie*, Stuttgart, 1880, p. 96.—29. VOIGT. "Ueber Impfschäden," etc., *Wiener medizinische Presse*, 1895, p. 294.—29*a*. WALLACE, ALFRED R. *Vaccination proved Useless and Dangerous*, Lond. 1889, p. 38.—30. WHEATON. *Trans. of the Path. Soc.* 1893, p. 140.—31. WHITE, WM. *Story of a Great Delusion*, 1885, p. xxxix.

PART IV

VACCINATION AND SYPHILIS

Introduction.—No part of the study of vaccination is more serious or more surrounded with difficulty than the attempt to estimate at their true value the conflicting statements concerning the transmission of syphilis by this operation. It is true that invaccination of syphilis is possible; but the facts brought before the Royal Commission (1889-1896) prove that, in England at any rate, the event is one of great rarity, and they do not justify any grave objection to the practice of vaccination.

Two methods, the statistical and the clinical, have been adopted to estimate the number of cases of vaccinal syphilis which actually occur. Of these the former is the less satisfactory, since it is liable to many sources of error; and although such figures as are available go far to prove that infantile syphilis has not been increased by vaccination, there is still stronger evidence against its frequency, in the fact that, although every alleged case of invaccinated syphilis brought before the Commission which had occurred between the years 1889 and 1896 was subjected to a searching inquiry, not one of them stood the test of an investigation into all the circumstances. During the years specified approximately five and a quarter million primary vaccinations were performed in the United Kingdom.

Of the cases vaccinated in 1889, and previous to this date, which were inquired into, one[1] was believed by Mr. Hutchinson and Dr. Barlow not to be a case of syphilis at all. In another (No. 141, App. ix. R.C.V.) the evidence was so indefinite that Dr. Barlow and I came to the conclusion that though there was some ground for the allegation, it was incapable of proof. This child had been vaccinated in 1880, twelve years before the inquiry was made; and at the time of the investigation there was no evidence of syphilis, invaccinated or otherwise acquired. Only three other cases were brought directly before the Commission in which there was *prima facie* ground for suspecting that syphilis had been communicated by vaccination,[2] and two of these cases had occurred twenty-five years previously.

If further evidence as to the rarity of the disease be needed, it may

[1] See Case No. 1 of the Commission series, and Case 90, L.G.B. series, Appendix ix. R.C.V.; also Hutchinson's *Archives of Surgery*, vol. i. No. 2, 1889, pp. 106 and 112.

[2] See Final Report R.C.V. pp. 110-114, and par. 424, p. 111.

be noted that amongst 30,000 patients at the Hospital for Sick Children, Great Ormond Street, a place where if such cases were of common occurrence they would be met with, Dr. Robert Lee has seen only one instance of supposed vaccinal syphilis; while at the East London Hospital for Children, Dr. Radcliffe Crocker has not seen or heard of one such case, although for many years he has been making special inquiries as to their occurrence.

Statistical method of inquiry.—During the last twenty years the number of deaths in England and Wales "registered" as due to syphilis has increased:[1] it has been suggested that this increase is due to syphilis inoculated at the time of vaccination.[2] The limit of age at which vaccination must be performed is, for this division of the United Kingdom, three months. As a matter of general experience vaccination is delayed as long as possible, so that any increase in the number of deaths from syphilis due to the operation would probably occur in children of more than three months old. Such however is not the case, the disease is most largely fatal during the first three months of life; so that whatever be the cause of this increase of syphilis, there is no evidence to show that it is due to vaccination.

In Scotland, where the age limit is six months, during the period 1855-1863, which immediately preceded that of compulsory vaccination, out of every 1000 deaths at all ages registered as from syphilis, 575 occurred during the first six months of life, and 109 between the ages of six and twelve months. During the period 1864-1875 the number of deaths registered as from syphilis during the first six months was 612; and in the period 1875-1887 it was 647. During the same periods the proportions of deaths registered as from syphilis between the ages of six and twelve months were 118 and 109 respectively. Thus in Scotland the number of deaths from this cause occurring during the second six months of life, when the results of vaccination would be most likely to declare themselves, shows no increase after vaccination had been made compulsory; the registered deaths during the months preceding the age limit for vaccination having at the same time increased.[3]

In Ireland the number of deaths from infantile syphilis has largely diminished during recent years. In 1864-1865 the average number of deaths so registered was 124; in 1887-1888 it was only 40.

In Leicester, where the practice of vaccination had fallen largely into disuse, the deaths registered as from infantile syphilis for the years 1883-1887 showed an increase of 69·3 per cent as compared with an increase of only 24·7 per cent for the whole of England and Wales for the same period. It need hardly be said that this increase is in no way connected with the disuse of the practice of vaccination; but it shows that the neglect of vaccination in Leicester has not been followed by any diminution in the number of deaths from infantile syphilis.

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[1] Final Report R.C.V. p. 103.

[2] Cf. also *Cow-Pox and Vaccinal Syphilis*, by Charles Creighton, p. 145, London, 1887, where the increase is attributed, not to syphilis inoculated with vaccination, but directly to vaccination itself, the results being erroneously called syphilis.

[3] Final Report R.C.V. pp. 101, 102. The statistics are given on the authority of the Superintendent of Statistics in the office of the Registrar-General for Scotland.

For the sake of comparison attention may be directed to the German statistics, from which it would appear that no case of vaccinal syphilis was recorded during the years 1889-1893 amongst a total of twelve and a quarter million vaccinations and re-vaccinations (30, 35), in the great majority of which "calf" lymph was used.

Whatever percentage of error is to be allowed in these statistics, it is evident from the above figures that they emphasise the fact, which, as we shall see, may fairly be deduced from clinical experience also, that the risk of inoculation of syphilis with vaccination is almost incalculably small.

Clinical method of inquiry.—Turning now to the clinical aspect of the inquiry, it is necessary to distinguish accurately between actual and alleged cases of vaccinal syphilis.

That many of the recorded cases are not syphilitic there can be little doubt. This may be said more especially of those which occurred in the early part of the century; but even at the present time cases are reported as vaccinal syphilis which, upon careful examination, do not appear to be of this nature (27). In those cases which I have had the opportunity of investigating, I hesitated to believe that the phenomena in question originated vaccination alone. They generally showed wide divergences from invaccinated syphilis so far as it is known; and almost without exception some extraneous factor was present in each case which determined the character of the phenomena which followed the operation. In some instances there was evidence of culpable negligence of those simple precautions without which no operation is justifiable, and without which any surgical procedure such as vaccination may well be followed by disaster (5, 32).

I have not obtained sufficient evidence in the course of my inquiries to lead to the conclusion that certain rare cases to which reference is here made are reversions to an original type of vaccinia; they appear rather to be abnormal results occurring in the course of a definite affection, such as sometimes complicate any of the acute specific fevers.

To illustrate these cases I would specially refer to (*a*) Mr. Hutchinson's paper on three fatal cases of gangrenous ulceration of the arm after vaccination (20); (*b*) case of simulated vaccination syphilis (21); (*c*) the various cases included under Section D in the Abstract of Reports by Inspectors of the Local Government Board, made by myself and Dr. Coupland; (*d*) Cases 52, 94, 109, 113, 195, 202, reported by myself; (*e*) series 139, investigated first by myself alone, and subsequently with Dr. Barlow; (*f*) finally, to the "Leeds Case," No. 1 of the Commission's series, probably the most important of all.[1] These are given in full in Appendix ix. to the Final Report of the Royal Commission on Vaccination, 1896. From these reports it will be seen that although in each case the invaccination of syphilis has been alleged, and, as in the Leeds case, the allegation has been stoutly defended, yet the conclusion arrived at, after carefully weighing all the facts that can be elicited, is that none of them was due to this infection. It was found that some were cases of gangrenous ulceration, some the result of vaccination in children suffering from congenital syphilis; and, whatever the origin of the lesion, each individual case presented facts which seemed to be incompatible with the view that the symptoms were those of syphilis inoculated at the time of the operation. The manifestations of syphilis are protean; and in doubtful cases no safe deduction can be made from isolated symptoms. Before any conclusion can be drawn as to the true nature of the disease, it is essential to take into consideration the complete history of the case, its evolution, the date of appearance, and the kind of lesions produced. It cannot be doubted that neglect of such precautions has led in many instances to confusion and to mistaken diagnosis. Amongst the cases inquired into by myself, I have found that the formation of a sore at the point of inoculation a week after vaccination, appearing rather to be syphilitic than vaccinal, the occurrence of periosteal swellings which arose a week after vaccination in a case unquestionably septic, the occurrence of cutaneous eruptions presenting "a certain suspicion of syphilis" during the second and third weeks,—have each in their turn been taken as evidence of invaccinated syphilis, without regard to the fact that a particular symptom isolated from all others is of small weight in deciding the true nature of a given case. Further, such symptoms become of even less value as evidence when they have appeared "untimely"—that is, at a moment when, from what we know of the natural history of the disease, the initial sore of syphilis would not have arrived at maturity, and at a period when neither secondary nor tertiary symptoms could have had time to declare themselves. Cases showing the difficulty of eliminating such sources of error will be found in Mr. Hutchinson's *Archives of Surgery*, vol. i. p. 97, and in the reports by myself to the Royal Commission on Vaccination, Nos. 109, 113, 207, 416, and others. It would not be possible here to enter into these cases in detail.

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[1] Cf. also Hutchinson, *Archives of Surgery*, 1889, p. 112.

In his evidence before the Commission (Sixth Report R.C.V. 1895, p. 159, Q. 21,854), Mr. H. H. Taylor put forward the following table of "alleged cases of vaccinal syphilis," at the same time expressing the opinion that it is impossible in many of them to say whether "the signs which followed vaccination were the manifestations of syphilis or cow-pox."

This table is too untrustworthy to be of any service in estimating the actual number of cases of vaccinal syphilis which occurred during the years specified; but it is important as showing the extreme difficulty of obtaining accurate information on the subject.

The danger of drawing any conclusion from it is well illustrated by the fact that, although Mr. Taylor handed it in as a table of alleged cases of vaccinal syphilis, Dr. Collins and Mr. Picton (4) allude to it as a list of cases of vaccino-syphilis; and both Mr. Taylor and Dr. Creighton use these same cases as evidence that the so-called vaccinal syphilis is nothing but cow-pox. No further testimony is needed to show the inextricable confusion of the whole subject.

English Cases of "Alleged Vaccinal Syphilis," taken from Mr. H. H. Taylor's Table. See Appendix Sixth Report R.C.V. 1895, p. 617. Foreign cases have been omitted.

N.B.—The references given have in some instances been amended.

Date.	Place.	Number of Cases.	Authority.	Remarks, T. D. A.
1. 1802	London	1	Letter from Mr. Smyth Stuart in Squirrell's *Observations on Cow-Pox*, 1805, p. 39.	No mention of suspicion of syphilis at place of reference. The words are, "I was led to consider the cow-pox virus possessed a specific scrofulous nature."[1]
2. 1859	Manchester	14	Whitehead, Third Report, Clinical Hospital, Manchester, 1859, p. 51.	Inconclusive. Evidence very meagre. No details given sufficient to exclude congenital disease. No facts given in support of the suspicion raised.
3. 1871	London	21	Hutchinson, *Illustrations of Clinical Surgery*, fascic. vi. pp. 115 and 122.	Recorded by Mr. Hutchinson as cases of vaccinal syphilis — as are also those marked †.
4. 1871	London	1	T. Smith, *Clinical Society's Transactions*, 1871, vol. iv. p. 53.	Probably a case of invaccinated syphilis, but report very incomplete. No mention of vaccinifer nor co-vaccinees.
5. 1872	London	1	Hutchinson, *loc. cit.* p. 126.	†
6. 1873	London	1	Hulke, *Med. Times and Gazette*, 1873, p. 153.	No details. Mr. Hulke said he had seen a case which he believed to be vaccinal syphilis. No facts given in support of the suspicion raised.
7. 1876	London	1	Hutchinson, *loc. cit.* p. 128.	† Should be two cases. Mother contracted syphilis from suckling her child; primary sore on nipple; symptoms followed two months later than in children. Father contracted disease from wife.
8. 1883	London	40	Transactions of the *Vaccination Inquiry*. Edited by M. D. Makuna. Part I. 1883.	Quite unreliable. Sixteen correspondents say they have seen cases, but no details are given.
9. 1883	London	1	Druitt, quoted by H. Lee: Holmes' *System of Surgery*, ed. ii. vol. iii. p. 349.	Case did not occur in England. No details. Dr. Druitt saw the case abroad and made a sketch of it.
10. 1889	London	2	*Archives of Surgery*, vol. i. p. 97.	Recorded by Mr. Hutchinson as not being vaccinal syphilis; although two were thought by some who saw them to have been syphilitic.
11. 1890	,,	3	Do., vol. i. p. 193.	
12. 1891	,,	1	Do., vol. ii. p. 213.	

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[1] Creighton, *loc. cit.* p. 113, states that the word "venereal" stood in the original, but was suppressed, and "scrofulous" substituted; the words "suspected venereal taint" appear in

Some further comment is needed on two of the above series, Nos. 2 and 8.

No. 2.—Dr. Whitehead (38) gives a table of sixty-three cases (out of a total of 2584 patients) which he believes to have been syphilitic; and out of this number fourteen are attributed to vaccination. In none of these cases is the condition of the vaccinifer or co-vaccinees mentioned; there is no evidence to show that they were examined: in three cases only is it definitely stated that the father and mother were healthy, and even as to these, no statement is made that either father or mother was examined. Deductions drawn from such uncertain data must obviously be liable to many fallacies.[1]

No. 8.—This series is useless for accurate purposes, no details are given in Mr. Makuna's Inquiry; sixteen observers say that they have seen cases of invaccinated syphilis (twenty-one cases), but their replies are very inconclusive, and there is nothing to show which of those who answered Mr. Makuna's "Inquiry" had seen particular cases, or whether more than one of them had seen the same case.

Clinical history of vaccinal syphilis.—The inoculation of syphilis at the time of vaccination may be due to various causes: (i.) To direct contamination of the lymph taken from a vaccinifer suffering at the time from syphilis (9, 28, 35). (ii.) To accidental contamination of the instrument or wound. (iii.) To infection from the vaccinator. It has been suggested (19) that infection might be conveyed by a vaccinator, suffering at the time from syphilis, blowing out the lymph from the capillary tube, but there is no evidence that such an accident has ever taken place.

In whatever way syphilis be invaccinated a certain definite sequence of events may be expected. These are as follows: if the person vaccinated be susceptible to vaccination the pocks may not at first show any departure from the normal course, but in some cases the pocks abort, and the pathological process seems to be at an end until the syphilitic virus asserts itself. If the pocks be irritated, or the condition of the tissues be such as to favour suppuration, the vaccinal sore may become inflamed, suppuration may occur, and the ulcers may for a time scab over and then break down again; but under any circumstances, whether the vaccination pursue a normal or an abnormal course, a true syphilitic chancre with indurated base eventually forms at the point of inoculation.[2]

Dr. Cory's experiments on himself, reported by Bristowe, Hutchinson, Humphry, and Ballard, throw valuable light on the clinical history of invaccinated syphilis; and the sequence of events in vaccinal syphilis may be studied from this case, which was carefully observed and recorded (33).

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a version of the letter published by Dr. Smyth Stuart two years after Squirrell's *Observations* were published. Cf. *An Address on Vaccination*, etc., by Ferdinand Smyth Stuart, Esq., London, 1807, pp. 9 and 68.

[1] Creighton (5) uses these cases as an argument in support of his view that vaccinal syphilis is not of "venereal" origin at all, but due "to the inherent although mostly dormant natural history characters of cow-pox itself."

[2] Fournier, *loc. cit.* p. 125. Cf. also table on page 609 for further references.

R. C. purposely vaccinated himself on four occasions from children known to be syphilitic. On the first occasion, in 1877 or 1878, vaccination was successful, but the vesicles matured early and declined after the fourth or fifth day. No syphilitic trouble followed. Some two years later he vaccinated himself again from a tainted source. Neither vaccinia nor syphilis resulted. About eighteen months later he repeated the experiment, again with negative results.

On the fourth occasion he was vaccinated in three places (34), from a child who was selected as being obviously the subject of congenital syphilis. She had suffered from thrush, snuffles, and a cutaneous eruption. At the time the lymph was taken from her arm she had sores on the right buttock and the left nostril; and there was still a cutaneous eruption, though not in the immediate neighbourhood of the vesicles, which were normal and not inflamed: they were shallow, however, and difficult to prick without drawing blood. The lymph was collected on a cleansed lancet, the utmost care being taken to avoid any admixture of blood. The next day the three insertions were red, with small areolas which declined gradually, and the arm was entirely healed in six days. On the twenty-first day a red papule formed at two of the points of inoculation: these slowly enlarged, and on the thirty-first day one began to desquamate. The papules continued to increase in size up to the thirty-fifth day, a slight areola being occasionally visible. On the thirty-fifth day a little yellow spot appeared in the centre of one of the papules, and by the next day a scab had formed over it. Two days later (the thirty-eighth day) the scab which covered this papule was removed, and a small ulcer was found beneath it. On this day the arm was seen by the late Sir George Humphry and by Mr. Hutchinson; both observers considered the lesions to be syphilitic. The diseased parts were then removed with antiseptic precautions, and five days later almost all tenderness had disappeared; but for the first time an enlarged and painless gland was felt in the axilla.

Next day, the forty-fifth, the lower wound was indurated, and the punctures caused by the needles, with which the edges of the wound had been united, had sloughed; and increasing pain was felt in the axilla. For the next four days the pain in the axilla was severe, and the glands were enlarged and tender; and on the fiftieth day, the constitutional symptoms having been gradually increasing, there was a distinct feeling of illness. Two days later, blue pill (5 grains daily) was taken with much benefit; but on the fifty-fourth day rheumatic pains were felt, followed within forty-eight hours by much soreness of throat; next day, the fifty-sixth, the cervical glands became painful; on the fifty-seventh day a roseolous eruption appeared on the forehead, the temples, the back of the neck below the ears, and the lower part of the abdomen, which lasted four days; after this date antisyphilitic treatment was fully carried out.

The subsequent history of the case shows that the experiment was only too successful.

be obviously syphilitic; or can the virus be communicated from a child apparently in good health?

ii. What is the actual vehicle by which the virus is transmitted?

iii. Given a healthy vaccinifer, can syphilis be communicated in the act of vaccination independently of the lymph?

iv. Can syphilis be communicated in lymph taken directly from the calf?

(i.) As regards the first proposition, none of the recorded cases seem to me to prove beyond doubt that a child not in the active stage of syphilitic infection can communicate the disease; though Fournier (16) and others appear to think that it is possible.

Mr. Hutchinson's cases (23, 29) have been accepted as evidence on this point; but it is possible that the infection may have been conveyed by the lancet from another child, and not from the vaccinifer at all.

With regard to this point it is most important to remember that, as has been stated (cf. p. 583), vaccination may pursue a typically normal course in a syphilitic child provided that it is not cachectic.

(ii.) The question of the actual vehicle by which the virus is transmitted has long been under discussion. M. Viennois (de Lyon) was of opinion that the virus is contained in the blood. It has been asserted by Barthelemy,[1] and later by Husband,[2] that it is practically impossible to collect lymph in the ordinary way which does not contain blood corpuscles; so that, if collected from vesicles on a syphilitic individual, apparent clearness of the lymph is no security (cf. Deduction, *d*, p. 608).

(iii.) The following cases have been mentioned by Voigt as supporting the view that syphilitic infection may be communicated from a child's co-vaccinees.

At Tauberbischoffsheim four children were vaccinated from an infant whose mother was a woman of the town: this child died shortly after being used as a vaccinifer. All four sub-vaccinees subsequently presented symptoms of syphilis; three were probably of syphilitic parentage, and inasmuch as the vaccinifer at the time the lymph was taken from its arm is said to have shown no sign of congenital disease, it is suggested that the fourth was infected from one of its co-vaccinees (1). The evidence is very inconclusive; especially as the physician, under whose care the vaccinifer was when he died, suspected some inherited taint. The vaccinifer seems to have been selected without regard to the ordinary precautions which should invariably be taken in every instance. Such instances show the importance in all cases of suspected vaccinal syphilis of investigating the history of the co-vaccinees, and of the vaccinifers in the direct line, for some generations; lack of information on these points must invalidate any deductions subsequently made as to the source of infection.

(iv.) It is probably impossible for syphilis to be conveyed by lymph taken directly from the calf, even though the calf had been vaccinated from a syphilitic child; it has been shown by Koch that the syphilitic poison is destroyed by passing through the animal, and there is no evidence to show that cattle are susceptible to this disease (18). The foregoing statement shows from clinical evidence that although it is possible to transmit syphilis in the act of vaccination, it is of very rare occurrence, and is not to be feared if ordinary precautions are taken.

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[1] Fournier, *loc. cit.* p. 112.

[2] Final Report R.C.V. 1896, p. 112, par. 430.

The disease is stated to have been transmitted from a syphilitic vaccinifer in some fifty series of cases during the last century (26). Even if this estimate be approximately correct, it shows that amongst the many millions of vaccinations, the danger to an individual of contracting syphilis through the operation is inappreciable; and that such indeed is the fact is borne out by a statement made by Mr. Hutchinson to me some little time ago that he had not seen a case of vaccinal syphilis for ten years —evidence as to its rarity more convincing than a multitude of statistics.

Differential diagnosis of vaccinal syphilis.—It remains to call attention (i.) to the main differences which have been found to exist between vaccinal syphilis and other lesions following vaccination; (ii.) to the points which may lead to the correct differentiation between invaccinated syphilis and vaccinia occurring in a syphilitic child; and, lastly, (iii.) to the points of difference between vaccinal ulceration and vaccinal chancre.

(i.) *The differences between vaccinal syphilis and other lesions which may follow vaccination* are well illustrated by the Leeds case,[1] which has been alluded to more than once. In this instance the child when vaccinated was nearly four months old. She was the third in the family, was at the time in good health, and had been previously so. The parents, the vaccinifer, and the co-vaccinees, so far as could be ascertained, were all healthy and without any signs of syphilis. On the sixth day some inflamed spots formed at the seat of inoculation; the inflammation spread rapidly, and towards the end of a fortnight two deep ulcers had formed with much dusky swelling round them. The inflammation and ulceration spread, and at the end of the month the child seemed ill. There was some false membrane on the velum and tonsils, and aphthæ appeared in the mouth; subsequently an ulcer formed on the upper eyelid, and one over the ear on the same side as the vaccination. Nine and a half weeks after the operation all the points of insertion had sloughed into one, producing a large unhealthy ulcer; and the two sores mentioned above were phagedenic. Nothing abnormal was noted in the mucous membrane of the mouth, and neither then nor subsequently was there any general eruption. The child's nutrition was fairly good. The case was treated with mercury, under the impression that it was syphilitic, and it seemed to improve. The sores on the eyelid and ear almost healed, but that on the arm remained unaltered, and "the mouth became very sore." About three weeks later the child was much worse, a large abscess formed on the right buttock and another over the upper part of the sternum. The skin over these parts was implicated, and appeared about to slough. Death resulted at the end of the fourteenth week after vaccination. The post-mortem examination did not throw any light on the nature of the case. No lesions of the viscera or bones were discovered. The arguments against the view that this was a case of invaccinated syphilis are:—

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[1] Case I., Appendix ix. to Final Report of Royal Commission on Vaccination; and evidence of Mr. Ward, Mr. Littlewood, and Dr. Barrs, Sixth Report of the R.C.V., Questions 23, 574-912; and Report by Mr. Hutchinson, *Archives of Surgery*, vol. i. p. 106.

(*a*) That the vaccine punctures began to inflame within a week; (*b*) that they did not develop into chancres; (*c*) that they did not cause any induration of glands; (*d*) that there was no general secondary eruption; (*e*) that the mother suckled the child and did not contract any sore upon the nipple; (*f*) that the chronology of events was quite unlike that of vaccinal syphilis; (*g*) that there was no evidence of syphilis in the vaccinifer; (*h*) that none of the co-vaccinees suffered in a similar way.

In view of all these negative data, the only satisfactory way of demonstrating that such a case was one of invaccinated syphilis would be to show that there was a probability of contamination of the lymph or of the instruments used in the operation. No evidence of this kind was to be obtained; so that the conclusion is justified that these, and similar cases, are erratic forms of necrosis following vaccinia, and are possibly due to sepsis, as cancrum oris and noma sometimes follow other acute febrile diseases, such as measles and varicella, without any ground for suspecting a syphilitic infection.

The following table is given for the sake of comparing the events in the case referred to with one of vaccinal syphilis, founded on those given by Prof. Fournier, *loc. cit.* p. 126:—

[TABLE

	Vaccinal Syphilis.	E. M. C. Leeds Case.
Incubation .	Chancre never formed before 15th day, generally after 3 weeks. (Usually end of 4th or even 5th week—Hutchinson.)	First sign of inflammation on 6th day. Ulcers formed during 2nd week.
Development	By the 21st day ulceration in its earliest development, or not yet commenced.	Ulcers fully formed by 14th day.
Vesicles .	As a rule all the vesicles are not affected, vaccination often aborts.	All the vesicles affected.
Inflammation	As a rule slight.	Great.
Loss of substance	Loss of substance superficial as a rule. Cf. Hutchinson, *Illustrations of Clinical Surgery*, 1878, pp. 121, 131.	Great. Vesicles sloughed into one large ulcer.
Discharge .	Scanty as a rule or absent. Generally forming scabs.	Considerable. Not drying into scabs.
Glands .	Enlargement always present, generally indolent, not inflammatory induration.	No induration of glands.
Secondary eruption	Roseolous eruption frequently present after formation of chancre, followed, at earliest 6 weeks later, by true syphilides.	None.
Tertiary symptoms	Gummata not generally present for many months after primary sore.	Large abscesses formed, surmised to be softening gummas, 12 weeks after vaccination.
History .	A history of syphilis in parents, vaccinifer, or co-vaccinees to be expected.	No history of syphilis in vaccinifer or co-vaccinees.

(ii.) *The differential diagnosis between vaccinal syphilis and the results of vaccination in a syphilitic child* in cases in which vaccination is either normal or abortive does not, as a rule, present any serious difficulty. But in those cases in which pus has been inoculated with the specific virus, or the pocks have been irritated and suppuration consequently set up, there may be some departure from the normal course of events.

I have recorded several important cases of this kind. In one the mother of the child had suffered severely from syphilis, and she had already lost one child from congenital disease. Her infant suffered after vaccination from severe inflammation round the pocks, which resulted in gangrene (see Case 202, App. ix. to Final Report R.C.V.) In another instance a child exhibited a general eruption during the first week after vaccination, and was shown at a London hospital two days later as a typical case of congenital syphilis: there was evidence to show that both parents had suffered from venereal disease (Case 326, App. ix. R.C.V.) Lastly, attention may be directed to Case 309, wherein, so far as can be ascertained, the vaccination pursued a normal course, and the child died of symptoms of inherited disease; the history of the parents gave the strongest support to the view that this diagnosis was correct.

The chronological order and sequence of events in these or similar cases may be seen in the following table compiled from Fournier, Hutchinson and others, and compared with a case investigated by myself:—

Symptoms and Sequence of Events.	Hereditary Syphilis.	H. C. Report No. 207, p. 397.
Evolution .	Irregular. Commencing as a rule with general symptoms.	Irregular. Ulcer at seat of vaccination formed by 12th day. No induration of base. Ulcer healed in 6 weeks without specific treatment. Evidence of general infection at the end of 5th week.[1]
Rash . .	Rash papular and pustular, often chiefly on face. Roseola on abdomen not the rule. Rash and excoriation round nates and scrotum common.	Rash papular and pustular, chiefly on face, chest, and arms. Not preceded by any roseola on abdomen.
History .	Family history of syphilis important.	Grounds for suspecting syphilitic infection in both father and mother.
	It is almost unknown for a child suffering from hereditary syphilis to inoculate its mother.	Mother suckled child without infecting her nipple.

(iii.) *Differences between vaccinal ulceration and vaccinal chancre.*—Allusion has been frequently made to vaccinal ulceration; and though unquestionably it appears to occur at times in children not obviously cachectic, my own experience has been that it is mostly the result of some morbid condition—as in Case 202, in which the child was unquestionably of syphilitic parentage; or to some extraneous source of irritation—as in Case 144, where the wounds were treated with castor oil, with buttermilk applied with a feather, with brewer's yeast, and with bread poultices. It is in fact wonderful that severe ulceration does not more frequently occur. I have been shown a case with ulceration, considered suggestive of syphilis, in which the wounds had been treated with cream applied with a feather which was picked up in the back yard and which had been left unwashed in the cream for some weeks. In another case buttermilk was applied to a piece of rag and left adherent to the wounds for some three weeks without being changed. I have also seen cases in which the vaccination wounds had been scrubbed and irritated by the edge of the sleeve saturated with the pus and blood in which it had been soaked for many days. These instances might be multiplied; but those given sufficiently indicate the fallacies which beset the opinion

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[1] Compare with table of symptoms in vaccinal syphilis on page 616.

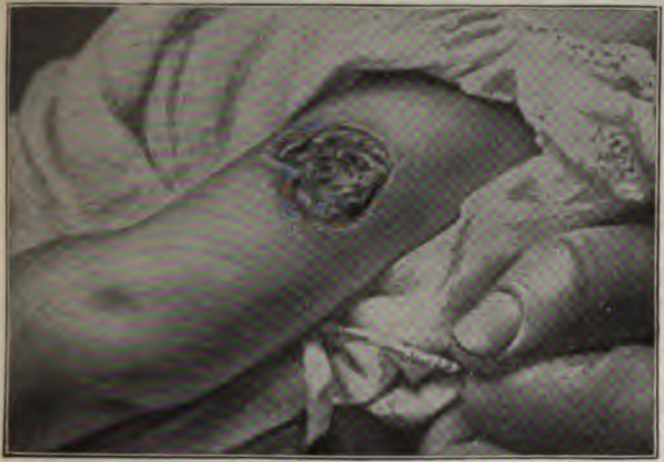
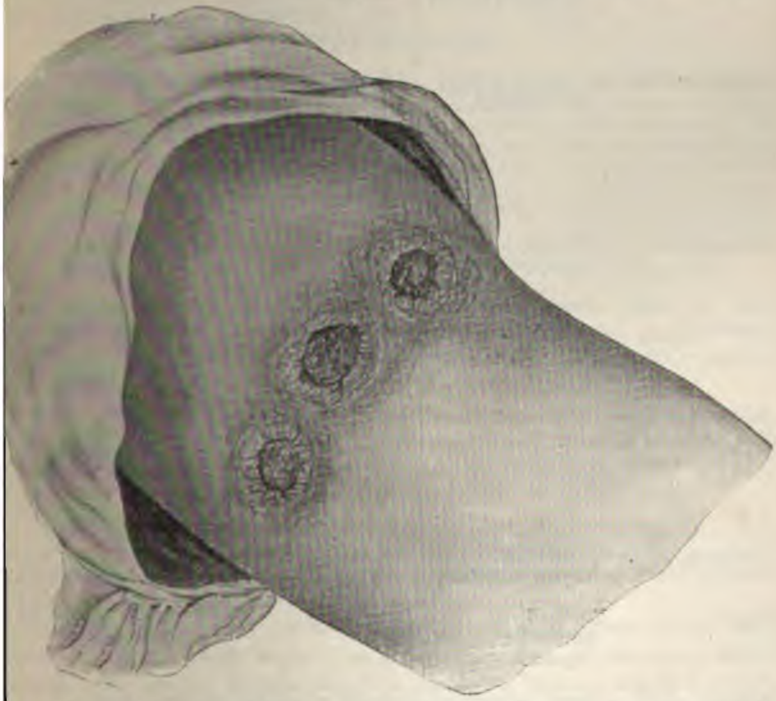


FIG. 11.—Vaccinal ulceration. From a photograph taken in the 2nd week after vaccination.



12.—Vaccinal Syphilis. Reproduced from a drawing of Mr. Hutchinson's case, *Illustrations of Clinical Surgery*, plate xxiv. Three chancres are situated at the point of vaccination. The vaccinal pocks went through their normal stages and healed well before the chancres developed. The drawing was made two months after vaccination, when induration was just commencing.

that cases of vaccinal ulceration taken without knowing the circumstances are either suggestive of syphilis, or "are manifestations of cow-pox," or necessarily indicate any analogy between the two disorders.

The ordinary features of vaccinal ulceration (Fig. 11) are shown briefly in the following table taken from an actual case, and placed side by side with those which have usually been observed (17) in vaccinal syphilis (Fig. 12):—

TABLE comparing Vaccinal Ulceration and Vaccinal Syphilis, with an actual case (see Figs. 11 and 12).

Generally observed Symptoms of Vaccinal Ulceration.		Case of J. W. P.	Vaccinal Syphilis.
1. THE ULCER			
Incubation	12 to 15 days.	14 to 16 days.	Generally upwards of three weeks, never less than 15 days.
Development	Ulceration fully developed by 21st day.	Ulceration well marked by 16th day, at its height on the 25th day.	Ulceration in its earliest development, or not yet commenced, about 21st day.
Vesicles affected	As a rule all vesicles affected.	All the vesicles (three) affected according to Dr. H. V.; one ulcer formed according to Mrs. P. the mother.	As a rule all vesicles not affected. Vaccination vesicles often abort.
Inflammation	Generally a prominent symptom.	Considerable.	As a rule slight.
Loss of substance	Great. Ulcer generally deeply excavated.	Great. Ulcer deeply excavated.	Loss of substance, superficial with rare exceptions. Much less excavated than a vaccinal ulcer. (Compare a case which was "probably on the verge of phagedæna," *Illustrations of Clinical Surgery*, Jonathan Hutchinson, 1878, at pages 126 and 131).
Discharge	Considerable; not drying into scabs.	Considerable; not drying into scabs.	Scanty or absent, nearly always forming scabs.
Edges	Punched out, perpendicular, irregular.	Punched out.	Not punched out, sloping to floor.
Bottom	Uneven, unhealthy-looking, sometimes sloughy.	Unhealthy-looking.	Smooth, even.

TABLE comparing Vaccinal Ulceration and Vaccinal Syphilis—*continued.*

Generally observed Symptoms of Vaccinal Ulceration.		Case of J. W. P.	Vaccinal Syphilis.
Base	Inflammatory induration.	Inflammatory induration.	Induration circumscribed, elastic, parchment-like.
Areola	Extensive. Diffuse inflammation, lymphangitis, cellulitis, erysipelas, and other inflammatory complications common.	...	Very slight, often inappreciable.
2. THE GLANDS			
Glands	Either no reaction or acute inflammation.	Not noticed to be enlarged.	Enlargement always present, indolent non-inflammatory induration.
3. THE ERUPTION			
Development	First appearance between the 9th and 15th days, always contemporaneous with vaccination.	First rash, red with some exudation noticed on 10th day after vaccination. Second rash, scaly, coppery, about 40th day.	At the earliest, appear first, 63 to 70 days after vaccination. (In Mr. Hutchinson's cases it varies from 42 to 63 days when untreated, and from five to seven months in those under mercurial treatment. (*Loc. cit.* p. 133.)
Relation to primary sore.	Not preceded by a typical vaccinal chancre.	Not preceded by a typical vaccinal chancre.	Always preceded by a chancre at the point of vaccination.
Clinical characters.	Of ordinary types (roseola, miliaria, bullæ, etc.); not lasting. No mucous tubercles.	No mucous tubercles.	Characteristic syphilides; persistent. Mucous tubercles often present.

Some further points of distinction between vaccinal and syphilitic eruptions will be found in detail on p. 565.

What I have stated above will have indicated some of the many sources of fallacy which have to be guarded against in the investigation of an alleged case of vaccinal syphilis; and the section on this subject cannot be better brought to a conclusion than by quoting the judicial statement made in the Final Report of the Royal Commission, 1896, p. 109, which is as follows:—

"The close resemblance in certain very rare cases of the results of vaccination, whether with calf lymph, or humanised lymph to those attributed to syphilis (a resemblance so close that it has caused in a few cases a difference of opinion whether the disease was syphilis or vaccinia), has led to the expression by Dr. Creighton of the opinion that there is some essential relationship between these two diseases. This, however, is a point of speculation almost it might be said of transcendental pathology upon which for practical purposes it is useless to enter. It must be sufficient to remark that, whatever may be the relationship alluded to, it exists, if it exists at all, equally between small-pox and syphilis as between vaccination and syphilis. For all practical purposes variola and vaccinia are both wholly distinct from syphilis, and their differences are, with the rarest exceptions, easily recognised. They are alike in being attended by affections of the skin and mucous membranes, and exceptionally by disease of the bones, eyes, and other parts, but in all these it is a question of resemblance and not of identity with which we have to deal."

REFERENCES TO PART IV. ON VACCINAL SYPHILIS

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Part V

Vaccination in Relation to various Diseases

Vaccination and tubercle.—The question of the possibility of the transmission of tuberculosis by vaccination has received much attention. M. Degive, at the Congrès pour l'étude de la Tuberculose, Paris, 1889, stated that it had been proved that the vaccine pustule could transmit tubercle; but no evidence was brought forward at the time in support of the assertion. When traced to its origin it was found to rest on an account given by M. Butel of some experiments performed by three Greek physicians, and on some well-known experiments made by M. Toussaint;[1] and not on any new facts brought to light by the speaker. The three Greek observers are stated to have inoculated two rabbits with lymph taken from a vaccine vesicle raised on a person suffering from "phthisis of the first degree." In one of the rabbits a tubercle was noticed at the point of inoculation at the end of twelve days, and after five weeks there was generalised tuberculosis. The author of these statements, in reply to my request for further particulars, expressed his regret that his notes were lost. M. Toussaint's experiments consisted in vaccinating a tuberculous cow on the vulva with lymph taken from a well-formed vaccine vesicle raised on a healthy child. On the seventh and eighth days—the pocks being then umbilicated—he took lymph and with it inoculated four rabbits, a pig, a cat, and a pigeon. Two of the rabbits were killed two months later, and were found to be suffering from tubercle at the point of inoculation, in the lungs, and in the lymphatic glands. The other two rabbits, killed just when they were going to die, were also tuberculous. The pig was killed 142 days after inoculation, and was found to be suffering from widely-distributed calcareous and caseous tuberculous nodules. The cat and the pigeon were killed on the sixtieth day and did not show any sign of tubercle.

These experiments are quoted because they are the only ones, so far as I am aware, which have been seriously advanced in support of the above statement made by M. Degive. They should be accepted with great reserve, as the sources of fallacy in their method are obvious. The first series, without more detail which unfortunately cannot now be given, can hardly be said to have any demonstrative value; the second series (M. Toussaint's) are inconclusive, as the vaccination was performed on a part which, if any tuberculous excreta were passed, could hardly fail to be contaminated. It may be pointed out that the cow selected was obviously tuberculous, and that experiments performed with lymph taken from the cow on the seventh and eighth days, and from vaccine vesicles in such a position and under such circumstances, can have little or no practical bearing on the transmission of tuberculosis in the ordinary course of vaccination.[2] If any further evidence were needed to show how little reliance can be placed on these experiments in support of the allegation that there is in fact a substantial danger of inoculating tubercle with vaccination, it may be pointed out—

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[1] The original communication (14) was made in 1881: "Note présenté à l'Académie des Sciences le 8 Août, 1881. Infection tuberculeuse par les liquides des sécrétions et par la sérosité des pustules de vaccin."

[2] In the Minority Report of the R.C.V., paragraph 219, p. 202, it is stated that "the experiments of M. Toussaint indicate the possibility of inoculating tubercle upon animals by vaccination" (reference being made to answer 22,714). But no new facts are brought forward.

1. That vaccine lymph is obtained from calves and not from adult cows; and even if it were obtained from adult animals, those obviously tuberculous would not be selected for the purpose.

2. That calves are very little liable to tuberculosis. It is stated by Fürst (20), on the authority of Pfeiffer, that only one case of "perlsucht" occurred during the first four months of life amongst 34,400 calves; and these numbers are borne out by the statistics of the abbatoirs at Augsburg and Munich, only one tuberculous calf being found amongst 22,230 at the former place, and even less frequently at the latter (29). Yet this almost inappreciable source of danger can be avoided by the simple precaution of not using the lymph from any calf until the animal has been killed and proved to be entirely free from disease. Such, indeed, is the practice in some parts of Germany.

Besides those mentioned above, a large number of experimental inquiries have been undertaken to ascertain whether the lymph taken from vesicles of a person undoubtedly suffering from tuberculosis contains tubercle bacilli, or is capable of transmitting tubercle to susceptible animals. Amongst them may be mentioned those of Josserand, Acker, Lothar Meyer, Straus, and Peiper. MM. Josserand's and Straus's papers contain references to inoculation experiments, and Peiper's article contains references to a considerable number of cases of tubercle accidentally inoculated. None of these observers has been able to detect tubercle bacilli in the lymph raised on tuberculous vaccinifers (human or bovine); and none of the animals inoculated with the lymph taken from Straus's cases showed even a suspicion of tubercle after inoculation. In Josserand's cases the post-mortem examinations gave negative results in forty-three of the forty-seven animals inoculated; not one gave conclusive evidence of tuberculosis, and one only had enlargement of the glands in immediate relation to the point of inoculation. The lymph in these cases was obtained by vaccinating individuals obviously tuberculous; and, when thus obtained, it was used for inoculating the animals experimented on by injecting it into the peritoneal cavity, under the skin, or into the anterior chamber of the eye; so as to produce the maximum result. In fact the experiments were done in a manner which could not possibly have its counterpart in vaccination. Further, it is important to bear in mind that it is very difficult to obtain tuberculous infection by simple scratching of the skin; and this fact, which is in accordance with common experience, has received confirmation from Prof. Chauveau's (15, 9) experiments. He found that in five instances in which he endeavoured to produce tuberculosis by means of inoculation through the medium of the skin, not only were the results negative, but also no sign of tubercle was found in any of the scars. It is probable that in those cases of local tubercular inoculation which occur after tattooing, cuts, and the like, the wound has always penetrated the skin so that the infection took place in the subcutaneous tissue. No undoubted case of invaccinated tubercle was brought before the Royal Commission on Vaccination; but Dr. Barlow has reported one case in which lesions, believed to be tuberculous, appeared in the skin of a child who had been vaccinated three months previously. The vaccination in this case pursued a normal course, and there were no tuberculous lesions affecting the vaccination sites or the lymphatic glands in the axilla on the same side as the vaccination. The child's father had died of some acute pulmonary disease of three months' duration, probably tuberculous.

A similar case is recorded by Marocco (26, 20). In this instance the child died of tuberculosis four months after being vaccinated with calf lymph. The pocks healed well, and subsequently disseminated red papules appeared; these suppurated, and caseous abscesses formed round the joints. No details are given of previous or family histories, so that this may have been no more than one of those coincidences which must occasionally occur after vaccination, without any causal relations between the operation and the subsequent event.[1]

I have seen only one case of death from acute miliary tuberculosis in an infant within the first few weeks after vaccination: in this case (No. 207, Appendix ix. to the Final Report of R.C.V., p. 397) the wounds healed completely, and about twelve weeks after vaccination the child died of acute miliary tuberculosis. The post-mortem examination showed that there was no induration in or around the vaccination scars, which were well and firmly healed; nor was there any enlargement of the axillary or cervical glands. There was, in fact, nothing in the condition of the scars, or of the glands in relation with them, to suggest that the vaccination and the tuberculosis were in any way connected.

From the facts which up to the present time have been brought to light, it would seem to be certain that the communication of tuberculosis in the course of vaccination is of such exceeding rarity that it is even doubtful whether it has ever been so transmitted. This latter conclusion has been arrived at by many observers both on practical and scientific grounds. Bollinger goes so far as to say that the inoculation of tuberculosis in vaccination is to be denied absolutely; and Dr. Heron, who has paid great attention to the question of the transmissibility of tuberculosis from one individual to another, informs me that he does not know of any recorded case in which the transmission of tubercle or lupus could rightly be attributed to vaccination.

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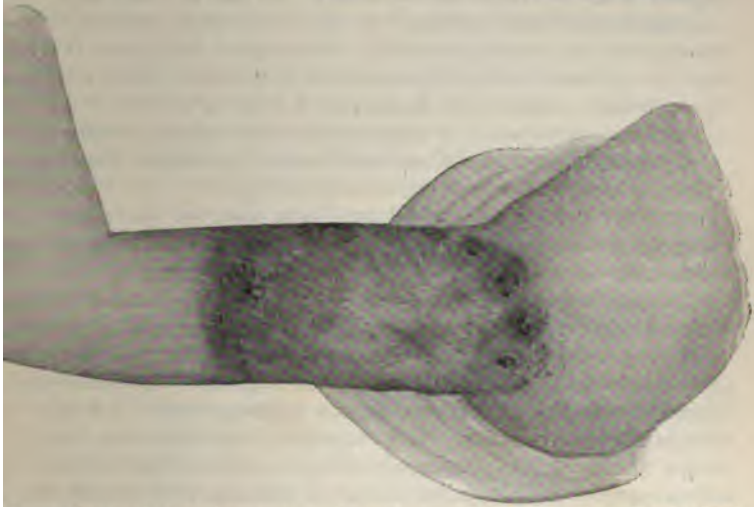
[1] In the Minority Report R.C.V. 1895, paragraph 219, p. 202, it is stated that "it has been found that tuberculous disease can be readily conveyed from infected animals to healthy animals or persons by the medium of infected animal-products such as milk." Although under certain circumstances this statement is correct, it has little or no direct bearing on vaccination. Tubercle bacilli have never yet been detected in vaccine lymph, even when raised on tuberculous individuals (such as could not possibly be selected as vaccinifers). And, further, the milk of tuberculous cows is only known to be infective when there is local tuberculous disease in the mammary gland. There is no evidence to show that the milk of tuberculous individuals in whom the gland is healthy either contains tubercle bacilli or is capable of communicating the disease. This opinion is shared by Dr. Sidney Martin, to whom I am indebted for information on the subject.

Vaccination and lupus.—Lupus affecting the seat of vaccination has been observed in some few instances; but it is much to be regretted that in none of the recorded cases with which I am acquainted has it been possible to determine with anything approaching to certainty whether the disease was invaccinated, or whether the case was merely an ordinary lupus attacking the vaccination scar; or even to show whether the lymph came from a contaminated source, or was presumably capable of exciting any but the specific effects of vaccination. Mr. Hutchinson (21) and M. Vidal (10) are of opinion that, in the cases recorded, there is no sufficient ground for believing that lupus resulted directly from vaccination, but that it was due to the patient's constitutional tendencies. There is some justification for this opinion; but there is no evidence to show that lupus itself can be transferred by inoculation from one person to another. M. Vidal, indeed, states that his numerous attempts to accomplish it have failed.

Dr. T. C. Fox informs me that he has seen a case in which lupus began in one of the vaccination scars shortly after the sore had healed. Subperiosteal tuberculous nodules, with a disseminated lupus, afterwards appeared; and after death it was found that the child was suffering from pulmonary tuberculosis. There is no record in this case of the source of lymph; and, as one other child in the same family died of tuberculosis, it is possible that this child was already tuberculous at the time of vaccination, and that the operation acted merely as the exciting cause of the acute disease: this often happens in children after the exanthems, and even after mechanical injuries. In the only case of post-vaccinal lupus, which I have myself seen and investigated ((2) and cf. Sixth Report of R.C.V., p. 141), the evidence was very inconclusive. The child was vaccinated in four places, two of the vaccination wounds did not heal completely, and two are stated not to have healed for two years; the lupus from which the child afterwards suffered is believed to have originated in one of the scars; and when the case was first seen five years later, the whole of the vaccinated area was involved (see Fig. 13). This child was the second of six children, and no member of the family was known to be tuberculous. The source of the lymph could not be traced. Cases reported by Lenander and Besnier are not more conclusive. The one was seen eighteen years after vaccination; the other more than thirty-four years afterwards. In Lenander's case vaccination is said to have been normal; and though lupus had commenced in the scar, and there was a small ulcer when the boy was ten years old, a doctor was not consulted about it until he was seventeen. When first seen by Lenander, the appearances of the original sore had been much altered by treatment; but the case was proved, on microscopic examination, to be tuberculous. No conclusion seems to be warranted from these cases, except that lupus may attack a vaccination scar, as it may attack any cicatrix; and, even supposing the local lesion to have no causal relation with vaccination, it is remarkable, seeing how frequently lupus occurs, that there are not more cases on record, he cause of the disease, it may and must always be difficult in ases rightly to apportion the precise effect of inheritance, circum- s, and vaccination : especially if, owing to feeble health, degenerate



-Lupus affecting the seat of vaccination. Drawn 9 years after the operation. For details of the case see p. 622, and Case 26, p. 242, Appendix ix. to Final Report R.C.V. 1896.

, and bad surroundings, vaccination has been followed by ulcera- glandular abscess, or some such complication likely to excite disturbance. A long inquiry into such a case will be found 374, App. to Final Report R.C.V. 1896. Further, the length e necessary for the evolution of the disease is so protracted that -powerful factors of inheritance, circumstances, food, clothing, and phthisis. How much of this is due to better diagnosis and to transference of cases from one class to another it is impossible to say; but that the increase is not due to vaccination may be inferred from the Leicester statistics, which prove to be a useful standard for comparison. In Leicester the increase in deaths from tabes mesenterica and scrofula during 1883-87, as compared with the years 1863-67, has been 25·8 per cent; the increase for England and Wales during the same period is 26·8 per cent; from this it may be inferred that, within reasonable limits of error, Leicester is, in this respect, as badly off without vaccination as the rest of England is with it. In the opinion of those best qualified to judge, the facts brought before the Vaccination Commission do not warrant the assertion that the increased mortality from the diseases under consideration is in any way due to vaccination (18).

Vaccination and leprosy.—It has often been asserted that leprosy can be, and has been, spread by vaccination; and some few individual cases have been brought forward as evidence in favour of the view. To determine whether this is possible it must be shown:—

1. That leprosy can be communicated directly by inoculation.
2. That leprosy bacilli can be detected in vaccine vesicles raised on a leper at the place where the skin is healthy.
3. That individual cases have been observed in which, from the evidence, there is good ground for believing that leprosy has been accidentally invaccinated.

The evidence on the first point, namely, the general question of the communicability of leprosy directly from one individual to another, is conflicting and contradictory. A case recorded by Dr. Hawtrey Benson (8) is important as giving ground for the suspicion that under exceptional circumstances the disease may be so communicated. In this instance, two brothers lived and slept together; one had contracted leprosy in the "Indies." He died, and three years later his brother, who had never been out of the United Kingdom but had worn his clothes, showed symptoms of the disease. This case is far more convincing than those which occur in countries where leprosy is endemic; though it does not justify any deduction as to the reality of the alleged danger of communicating the disease by vaccination. So far as the evidence goes at present it must be considered extremely doubtful whether the disease has ever been communicated directly or indirectly in the ordinary course of this operation.[1] Notwithstanding all that has been said by those who are of opinion that the increase in leprosy, which has occurred in some of the places where the disease is endemic, is largely due to vaccination, not one case in which there was any sufficient evidence to justify such a statement was brought before the Royal Commission of 1889-96. On the contrary, those who have had the widest experience and the best opportunities of forming a correct judgment—such men as Dr. Hansen of Bergen, and Dr. Beavan Rake, medical superintendent of the Leper Asylum at Trinidad—do not consider that any such inference can be drawn from the data which are available. These opinions, weighty in themselves, are supported by the fact that in New Zealand, Iceland, Norway, and India, leprosy has steadily declined (19), although vaccination has been widely practised; while in the Sandwich Islands it has at the same time largely increased. Dr. Hansen has never seen a case of invaccinated leprosy; he informs me that in 1890 he sent out a circular to all physicians in Norway, asking whether they had observed any case of leprosy occasioned by vaccination. This inquiry failed to trace a single case in which there was ground for believing that leprosy had been so caused. The importance of such a statement is obvious when it is remembered that vaccination is efficiently carried on throughout the country.

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[1] The whole question will be found fully discussed from the scientific point of view in the *Journal of the Leprosy Investigation Committee*, i. 5-11, 130, 141; iii. 90; iv. 32-41, 72, and from the opposite side, in the *Recrudescence of Leprosy and its Causation*, by W. Tebb. London, 1889. See also Beavan Rake, *Medical Record*, New York, 1893, vol. xliv. p. 705, and *Report on Leprosy for the year* 1892, Trinidad, 1893. Also Phineas Abraham, *Trans. VII. Internat. Congr. of Hygiene*, London, 1892, vol. i. p. 384; and in the present volume of this *System*, p. 41.

To prove that there is *prima facie* ground for believing that leprosy may be invaccinated, reference has been frequently made to the following experiments made by Arning (3, 4). He inoculated the left forearm of a native Hawaiian with a portion of leprous nodule; a month later the man suffered from pain in the left shoulder, elbow, and wrist, with painful swelling of the ulnar and median nerves. During the next six months the neuritis gradually subsided and a small leprous nodule formed at the point of inoculation. Leprosy bacilli were present for six months. Two and a half years later the symptoms of leprosy were definite; and a year afterwards the disease was at its height. The fallacy of drawing any deduction from such a case, to prove the danger of inoculating leprosy by vaccination, is too obvious to need comment; for, apart from the fact that vaccination does not consist in inoculation with leprous tissue or cultures of leprosy bacilli, the man came of a leprous family, and lived in a place where leprosy was endemic. Even Dr. Arning himself does not appear to consider that the case proves conclusively that leprosy was inoculated.

Inoculation experiments have been made by other competent observers, especially by Danielssen and Hansen; but the results were entirely negative.

Arning (5) detected leprosy bacilli in the lymph of vaccination vesicles raised on the skin of an advanced case of tubercular leprosy; but he did not detect any in lymph from two cases of anæsthetic leprosy. On the other hand, Beavan Rake (7) and Buckmaster (24) examined a large number of cases in a similar manner, and in most cases did not find any trace of bacilli. In the cases in which the part vaccinated was obviously diseased they found suspicious-looking rod-like bodies; but, as Beavan Rake states, even if the doubtful cases be admitted as evidence that leprosy bacilli are to be found in a vaccine vesicle raised on a patch of tuberculous leprosy, it has no bearing on the question at issue; since no responsible person would think of vaccinating a leper in an affected part, and using lymph from vesicles so obtained for further vaccinations.

The conclusions these observers arrived at are as follows:—

1. That the alleged cases of transmission of leprosy by vaccination are open to serious doubt.

2. That, assuming the presence of leprosy bacilli to be necessary to produce leprosy, no danger need be apprehended from the vaccine lymph even of an actual leper; provided he be vaccinated on healthy skin.

Turning from the experimental to the practical side of the question the evidence is even less precise and conclusive. Two series of cases have been repeatedly quoted as giving some ground for the suspicion that leprosy might be communicated in the ordinary process of vaccination. The first of these cases was recorded by Prof. Gairdner[1] and is as follows:—

Dr. X., living in a tropical island where leprosy was endemic, vaccinated his own son from a native child, and from his own boy in turn vaccinated a third child. Both the latter in after-years suffered from leprosy. The native child was said to have come of a leprous family, and Dr. Gairdner writes that he "understood (though perhaps not definitely so stated) that leprosy had declared itself in the native child after vaccination"; of this fact, however, there was so much uncertainty that in a subsequent letter to the *British Medical Journal* (13) he modified this statement, and says that the doctor's child was vaccinated from a native child who was "probably not an actual or apparent leper." Thus in this much-quoted case there is no evidence that the children, who some years later became lepers, were in fact vaccinated from a child suffering at the time from leprosy. Neither is it known that the latter subsequently became a leper. Again, there is no information as to the date or situation of the first appearance of the leprosy; and during the time which intervened between vaccination and the development of the disease the children appear to have been living in a country in which leprosy was endemic. So much attention would not be called to this case were it not that it has been almost invariably quoted as one in which the two boys who suffered from leprosy had been vaccinated from a native child who afterwards became leprous;[2] and much greater weight has been attached to it on this account than it rightly deserves.[3] The other classical cases are reported by Daubler (16).

Two women were vaccinated from a patient who subsequently died of tuberculated leprosy. In both instances leprous tubercles first appeared on the forehead and cheeks; in the one case eighteen weeks, and in the other about eight weeks after vaccination. They were not seen by Daubler until some years later (probably about 3½); and there is no evidence to show that the vaccinifer was leprous at the time when vaccination was performed: nor in either case was there any evidence that the disease began in the vaccination scars, or subsequently affected them. It is worthy of note that leprosy appeared in both cases in less than five months; and Dr. Beavan Rake remarks that clinical experience does not warrant the belief that a disease so essentially chronic as leprosy is produced so soon after inoculation. Other similar examples might be given; but the above will suffice to show that it is doubtful whether leprosy can be inoculated even under exceptional circumstances. Should this possibility, however, be proved, the disease could hardly be inoculated under the conditions which occur in vaccination; since, apart from the fact that a person suffering from leprosy or coming of a leprous family would not under any circumstances be used as a vaccinifer, there is ground for believing that vesicles developed on healthy skin do not contain the specific virus capable of communicating leprosy.

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[1] "A Remarkable Experience concerning Leprosy," etc., *British Medical Journal*, vol. i. 1887, p. 1269. I have made every effort to trace the vaccinifer in this case, as it is one not only of scientific but of practical interest. Dr. X. is dead: Mr. Racker, who wrote to Mr. Tebb (30) saying that he knew all about the case, gave the wrong initials for the father and the wrong name for the school at which the boy had been, so that his statement requires confirmation: neither Dr. Gairdner, Dr. Buckmaster, Dr. Beavan Rake, nor Mr. W. Tebb know more of the case than stated above. I have not yet received any reply to the inquiries I have addressed to Mr. Racker and Dr. Pasley, who both speak as though they were acquainted with the circumstances.—T. D. A.

[2] Cf. Beavan Rake and Buckmaster, *Journal of Leprosy Investigation Committee*, No. 4, p. 32; *Report of Leprosy Commission in India*, Appendix I. p. 414; Beavan Rake, *Medical Record*, New York, *loc. cit.* p. 708; Phineas Abraham, *loc. cit.* p. 6, and many foreign periodicals and monographs.

[3] Cf. C. F. Carter, *Leprosy and Vaccination in British Guiana; Journal of Leprosy Investigation Committee*, No. 4, p. 39; and Phineas Abraham, *loc. cit.* p. 3, note.

Vaccination and cancer.[1]—There is no authentic case on record in which cancer has resulted from vaccination; neither have I seen nor been able to trace any case of cancer affecting the vaccination scar. No mention would be made of the subject, were not cancer one of the diseases the increase of which has been attributed to vaccination (32).

Apart from this clinical evidence, which is very strong, the statistical evidence is still stronger; as may be seen from the following facts:—

1. The mortality from cancer during each quinquennial period of the first fifteen years of life has decreased.[2]
2. The increased mortality from cancer is greatest at the period of life furthest removed from vaccination.
3. The whole of the recorded increase in cancer has taken place in inaccessible cancer; that is, under circumstances in which exact diagnosis is difficult.
4. There has been practically no increase of cancer in accessible parts.

The whole subject has been ably worked out by Mr. George King, actuary of the London Life Office, and Dr. Arthur Newsholme (28); who, after examining all the evidence, draw the conclusion that the increase in cancer is apparent only, and is due to improvement in diagnosis and more careful certification of the causes of death.

Vaccination and epizootic disease.—No case of epizootic disease resulting from vaccination, or associated with it, has, so far as I am aware, been recorded in this country. Three cases of aphthous stomatitis occurring during the vaccination period, and in many ways resembling aphtha epizootica (foot-and-mouth disease), came under the observation of Dr. L. Voigt (31) of Hamburg; but inasmuch as many similar cases occurred in the neighbourhood, and there was also an outbreak of the affection amongst the cattle, there does not seem to be any ground for supposing that its occurrence in the vaccinated children was anything more than a coincidence: of the three children mentioned one had temporary discomfort, a second died of cholera with its father, and one only was seriously ill from the symptoms in question. This child suffered severely with high fever, stomatitis affecting the lips, tongue, and gums; the attack began on the tenth day after vaccination. A dusky papular eruption, which subsequently caused much irritation, appeared first on the lips, cheeks, and genitals; later it spread over the whole body, and ended in a severe folliculitis: this was complicated by bronchopneumonia. The child eventually recovered, vaccination having pursued a normal course.

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[1] Objection may be raised to the use of the word "cancer" as too vague. It is the term used by Mr. A. R. Wallace. Here it is not restricted to its technical meaning, but includes all forms of neoplasm.

[2] Final Report R.C.V., par. 391, p. 102.

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CONCLUSION[1]

General considerations.—The foregoing pages have shown that the danger from vaccination, as at present practised in the United Kingdom, is in individual cases very small; from invaccinated disease it is almost nil: and although in a fractional percentage of cases grave complications arise, in almost every instance they are due to inflammatory or septic affections such as are common to all wounds, and are found to depend far more on various extraneous circumstances than on any properties inherent in the lymph itself. Serious results, the direct consequence of constitutional affections such as generalised vaccinia, or of cutaneous eruptions such as impetigo or eczema, will probably continue to occur in some few cases from causes which cannot at present be foreseen; but, as has been shown, they are exceptional and their number small.

Children after vaccination are at all times liable to suffer from various harmless rashes of an erythematous or urticarial type, which, though for the most part free from danger, not infrequently give rise to considerable distress. Children are peculiarly liable to such eruptions from any cause which produces local irritation or disturbance of the digestive system. It is unlikely that any precautions in the selection of lymph would materially lessen the number of such cases; but it is essential that those who have the care of vaccinated children should be scrupulously exact after the operation in avoiding all extraneous sources of irritation to the wounds, more especially in those children who are known to be liable to eczema or other eruptions. If the instructions to public vaccinators under contract issued by the Local Government Board (1888) are carried out in the spirit as well as in the letter,—if the child be healthy, its circumstances wholesome, the lymph carefully selected and properly used, and if reasonable care be exercised after vaccination,—there is no doubt that the dangers of the operation are extremely small.

The various sources of risk, and the safeguards which they suggest, may be considered under the following headings:—The child and its circumstances; the treatment of the arm; the lymph, and methods of storing it; the vaccinator, and methods of vaccination.

The Child.—*Age.*—Although there is good ground for believing that under favourable conditions vaccination may be carried out successfully on infants of a few days old, the custom in some infirmaries and lying-in institutions of vaccinating children shortly after birth is not infrequently productive of dangerous complications; and the practice[2] is to be discouraged except at times when there is danger from small-pox: in this case the infant should, if possible, be kept under observation until the arm is healed.

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[1] This section is largely founded on a memorandum prepared by Dr. Barlow and myself for the Royal Commission on Vaccination 1896; and reference is frequently made to the recommendations of the Commission, *q.v.* Final Report R.C.V. pp. 113-116.

[2] Final Report R.C.V. p. 115, par. 441.

There are two obvious sources of danger in vaccinating very young infants.

i. A considerable number of the children born in our workhouses, infirmaries, and lying-in charities are born under circumstances which entail distress and disgrace on the mother; consequently they are often feeble, and sometimes diseased.

ii. The mother may take her discharge and leave the institution just at the time when the child's arm is most inflamed; thus she may return to conditions of life which cannot fail to be harmful to the child.

If, on account of the prevalence of small-pox, it be necessary to vaccinate newly-born children, it is unreasonable and probably harmful to vaccinate in four or five places[1]—to give, that is, the same dose of the virus to a newly-born infant as would be given to an adult man; such a procedure is contrary to sound principles of therapeutics. Yet it may be inadvisable that a child, vaccinated in one place only, should receive a certificate of successful vaccination; and a parent, whose infant was thus vaccinated, might be required to have it vaccinated fully at the expiration of a year from the first operation.

Previous health of child.—In many cases which I have inquired into, the child, previous to its vaccination, had been suffering from some ailment which could not fail to affect its general health. Among these may be mentioned convulsions, diarrhœa and vomiting, scrofulous glands, eczema, and so forth. Again in several cases the child had just been weaned, or put on some new kind of food, fed on unsuitable food, or fed insufficiently. The vaccination of such children is contrary to the regulations issued by the Local Government Board. Care must be taken to select children for vaccination; and not to perform the operation, as sometimes is the case, on children who are obviously unfit. If the time limit for vaccination be extended to six months it will give vaccinators more freedom in this selection, and enable them to defer the operation in cases in which the child's health is uncertain.

Circumstances.[2]—There is considerable risk (*a*) in bringing children to be vaccinated from houses in which there are cases of acute infectious disease: (*b*) in bringing them at the time of vaccination into direct or indirect contact with infectious disease: (*c*) in exposing them to possible infection from sloughing or open wounds, purulent ophthalmia, or discharges of any kind: (*d*) in subjecting them after vaccination to unhealthy conditions such as result from gross sanitary defects. Cases of vaccinal injury resulting presumably from each of these causes have been investigated and recorded. No open wound would be expected to pursue a normal course under such conditions; but persons responsible for the care of children among the poor often, from ignorance or negligence, disregard the most ordinary precautions.

It is desirable that simple instructions on these essential points should be given to every person who brings a child to be vaccinated;

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[1] Final Report R.C.V. p. 115, par. 441.

[2] *Ibid.* par. 445.

and that the form of such instruction should not be left, as it is at present, to the individual vaccinator. Some public vaccinators give careful instructions, as a matter of routine; but the practice is not general.

Attention should be called to the fact that whereas inquiries were made for the Commission into cases of alleged vaccinal injuries in all parts of England, not a single case amongst the well-to-do classes has come under the notice of Dr. Barlow or myself. With few exceptions the cases of injury have occurred amongst the poor and ill-fed, living under conditions so insanitary that it is well-nigh impossible that the children could be healthy. In this class the lives of infants are exposed to far greater dangers than in the wealthier classes; and even a trivial operation such as vaccination must be attended with a certain amount of risk, the risk being dependent far more on the condition of the child than on the nature and normal effects of the operation. For this reason, among others, it is desirable to discourage the practice of very early vaccination, and to extend the age limit from three to six months; so that weakly infants may have had time to grow more vigorous, and inherited disease, if any, will have had time to declare itself.

Treatment of the arm.—*Treatment of Insertions.*—Risk is often incurred by parents who, in the desire to lessen the severity of vaccination, wipe the lymph off the arm without due regard to the manner in which this is done; dirty fingers or dirty pocket-handkerchiefs are used, and the result often is irritation of the parts, excessive inflammation, glandular abscess, or some septic complication.

Treatment of vesicles.—One of the most frequent causes of vaccinal injury is due to the ignorance of the parents, and their disregard of the most elementary rules of cleanliness. Considering the variety of decomposable substances which are applied to the vaccination vesicles, and in a manner well calculated to accelerate decomposition, it is remarkable that the harm done is not greater than it is (cf. Vaccinal Ulceration, p. 614). It cannot be doubted that so long as such ignorance prevails as to the importance of cleanliness and the avoidance of mechanical irritation of the wounds, cases of injury will occur from time to time. The only way to combat these dangers is to instruct the parents in the care and treatment of the child before and after vaccination.

Shields.—It is probable that in many cases severe inflammation is caused, or certainly aggravated, by the use of shields. The shield is apt to rub the scabs off the vesicles and to produce an open sore. This danger is further aggravated when these shields are foul with pus from old vaccination wounds, as they not infrequently are kept and used for one child after another without being cleansed. In all cases the use of shields should be discouraged.

Dirty sleeves.—A similar source of danger is that of allowing a pus-soaked sleeve to rub into and irritate the vaccinal wounds. Ulceration and suppuration frequently arise from this easily removable cause.

Opening of vesicles.—As has been pointed out, the majority of cases of erysipelas occur after the first week; but I am not able to produce definite proof that the risk of inflammatory complications is increased if the vesicles are carefully opened. It would seem, however, to be desirable that this should be avoided as far as possible.

Inspection of arm.—Great hardship is sometimes inflicted by requiring parents, under a penalty of a fine, to bring their children on the eighth day for inspection. I have seen children brought to the vaccination station in driving snow and bitter wind, just at a time when they should have been kept warm and well protected. Such exposure is a serious element of risk. If the age limit were extended to six months, and the obligation for inspection removed, it would be possible for children to be vaccinated during the warmer months only, and the vaccinator would be able to excuse attendance on the eighth day at his discretion; or it might possibly be arranged for the vaccinator during the winter to inspect the children at their own homes.

The Lymph and method of storing.—*The Lymph.*—In a small proportion of cases the lymph has been found primarily and directly responsible for vaccinal injury. In these cases the fault generally lies in the application or use of the lymph. Certain exceptional cases have, however, occurred in which, although as far as could be ascertained the lymph was normal, some abnormal result—such as generalised vaccinia—has followed its use.

Sources and preparation.—It has not been possible to determine with any precision the relative frequency with which complications have followed the use of calf or of humanised lymph, or the use of lymph stored on points, in tubes, or as a conserve. Abnormal results occasionally follow the use of each of them; but as there has been no possibility of determining the total number of vaccinations performed in each way, there are no data for ascertaining the relative results of the several methods respectively.

The general impression left upon me by my inquiries is that vaccination direct from the calf tends to produce more severe inflammatory reaction than that which has been humanised; although there is no reason to believe that serious inflammatory or septic complications follow its use more frequently than they do the use of humanised lymph.

There is a widely-spread desire for an increased supply of calf lymph, and the desire seems to be a reasonable one. The existing Institution for the gratuitous supply of calf lymph is on too small a scale to meet the demands made upon it; and, vaccination being compulsory, it has been recommended by the Royal Commission on Vaccination that steps should be taken to provide an adequate supply of calf lymph for the use of those who prefer it.[1]

Storage of lymph.—From a theoretical point of view the storage of lymph in a dry state has doubtless great advantages; but in practice it is found less satisfactory than storage in tubes. Points may be dried without adequate protection in the dust-laden atmosphere of a crowded waiting-room; or carried about in the pocket merely wrapped in a piece of paper; or after use they may be recharged and used again without proper cleansing and disinfection. It seems, therefore, that the theoretical advantages of points are more than counterbalanced by the practical objections.

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[1] Final Report R.C.V. p. 113, par. 437. This recommendation will probably be very shortly carried into effect.

The storage of lymph, treated with glycerine, in tubes[1]—each tube containing only sufficient lymph for one vaccination—is probably the method least open to objection. It is of practical importance that only sufficient lymph for one vaccination should be contained in each tube, as serious results sometimes occur from the use of a tube of lymph which had been opened for a previous vaccination.

Vaccination and the vaccinator.—*Methods of vaccination.*—Cases of severe inflammation, abscess, erysipelas and septic infection have been known to follow the use of some mechanical vaccinator, or of the Cooper Rose needle. With adequate sterilisation such mechanical contrivances to shorten the process of vaccination would do no harm, and might serve a useful purpose; but they do not and hardly can receive the vigilant attention which is required to keep them surgically clean. Their use should therefore be strongly condemned; and attention should be called to the fact that it is essential that instruments used in vaccination should be as carefully sterilised as for any other operation. Nothing but an ordinary lancet or needle should be used, and the instrument should be much more thoroughly sterilised than is now frequently the case; preferably by immersion in some antiseptic or in boiling water, and by wiping each time, after use, on a fresh piece of sterilised wool.

Postponement of vaccination.—In all cases in which vaccination has been postponed it is desirable that a certificate, stating the causes of postponement, should be produced at the time when the child is subsequently vaccinated; so that the risk of taking lymph from the vesicles of a child known to be unhealthy may be rigidly excluded.

Position of pocks.—Ulceration not infrequently results from placing the insertions so near together that the vitality of the tissues between them is destroyed, and a slough is produced. This risk is easily obviated by not putting the insertions too close together, and by not making as many as four insertions in very young infants in whom the space is more limited.

Repeated vaccination.—In a few cases there is ground for believing that harm has resulted from repeating vaccination in a child a week after the first attempt, when the first vaccination had proved unsuccessful. It appears desirable that vaccination should not be repeated until at least four weeks have elapsed since the date of the first insertion.

Vaccination stations.—The use of surgeries as public vaccination stations should be discouraged, the performance of vaccinations in places to which every kind of infectious disease is admitted being of necessity fraught with considerable risk to the infants.

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[1] Cf. evidence before the R. C. on Vaccination by Dr. Copeman, and *Jour. of Pathology and Bact.* May 1894.

Certificates of vaccination.—There seems to be a certain amount of hardship involved in the fact that in the case of a private patient a certificate of successful vaccination may be, and sometimes is, given for a result which would not be accepted, and rightly so, by a public vaccinator. Instances occur in which a certificate of successful vaccination has been given by a private practitioner for one insertion; whereas four insertions would be made by the public vaccinator. It is obvious from this that a certificate of successful vaccination has no definite meaning, and does not necessarily show that a child has been properly vaccinated. It is desirable that every certificate of vaccination should specify the number of successful insertions.

Public vaccinators.—A general impression prevails that it is no part of the duty of a public vaccinator to attend to a child in case of any serious consequences of vaccination; at the same time some vaccinators gratuitously devote a large amount of time and care to a child suffering from some vaccinal complication, although they themselves are entirely free from any blame in the matter. It seems reasonable that it should be part of the duty of the vaccinator to attend any child who may be suffering from the results of the operation; but also that he should receive suitable remuneration for so doing. The fee which he receives for the operation cannot be considered as adequate remuneration for attendance on a child, it may be, for two or three weeks.

District nursing in regard to vaccination.—In populous districts, and in places where the services of a trained nurse are available, great benefit might result from having a competent person to act under the direction of the vaccinator, and to visit at regular intervals such cases as at the first inspection might be found abnormal. Many cases of the inflammatory kind might be quickly relieved by boracic lint, fomentations, or simple antiseptic methods properly applied. Moreover, a trained nurse might render material service in instructing the poor in due cleanliness, and in the avoidance of injury to the arm in dealing with their vaccinated children; and could give timely warning of the danger of sanitary defects or of exposure to infection from the specific fevers. Many accidental complications might thus be avoided.

Summary.—To secure successful vaccination, cleanliness, in the surgical sense, the careful selection of lymph from healthy children whose antecedents are known if humanised lymph be used, or the examination of the calf after death if calf lymph be used, and the postponement of vaccination on all feeble, cachectic children, or on those who are suffering from cutaneous eruptions, are essential. If these simple precautions be honestly carried out, the risk of invaccinated disease, or of any complication resulting directly from vaccination, will in the great majority of cases be obviated.

Since, with few exceptions, the complications which arise are not peculiar to vaccination, it is unnecessary to speak at length about their treatment. The most important points to remember are to keep the pocks uninjured, dry, and clean. They may be dusted, if necessary, with starch and iodoform powder, or with gallate of bismuth. If ulceration occur it may be necessary to make stimulating application to the wound, such as solution of chloride of zinc (gr. 10 to 40 to the ounce), or solution of hypochlorite of soda; but as a rule careful washing with warm water, or with a solution of boracic acid (gr. 20 to the ounce), will suffice without any more powerful application.

The treatment of such complications as syphilis, erysipelas, glandular abscess, eczema, impetigo, do not call for special comment. There is nothing in them peculiar to vaccination, and they may be treated without reference to the foregoing operation, provided only that the pocks themselves be kept free from injury, and in a healthy state. Lastly, it is above all things necessary that the child's general health should be attended to, and that it should not be vaccinated immediately after weaning, or after any other important change has been made in the method of feeding. There is a general disposition to regard vaccination as so trivial an operation that no precautions are necessary to ensure the well-being of the child, and to forget that the local pock is but the expression of a constitutional disturbance affecting a change in the whole being of the individual under operation.

T. D. Acland.

LIST OF SPECIAL WORKS OF REFERENCE

The following works, most of which have been frequently quoted, will be found to contain a great number of references to the literature of vaccination, in addition to those already given in this article:—

1. Bohn, Heinrich. *Handbuch der Vaccination.* Leipzig, 1875.—2. Creighton, Charles. *Natural History of Cow-pox and Vaccinal Syphilis.* London, 1887.—3. Crookshank, E. M. *History and Pathology of Vaccination.* London, 1889.—4. Fournier, Alfred. *Leçons sur la syphilis vaccinale.* Paris, 1889.—5. Fürst, D. L. *Die Pathologie der Schutzpocken-Impfung.* Berlin, 1896.—6. Longet, Ernest. *Dictionnaire encyclopédique des sciences médicales*, article "Vaccine." Paris, 1886.—7. Lotz, Th. *Variole et Vaccine.* Bâle, 1880.—8. M'Vail, John. *Vaccination Vindicated.* London, 1887.—9. Peiper, Erich. *Die Schutzpocken-Impfung.* Wien, 1892.—10. Seaton, E. *A Handbook of Vaccination.* London, 1868.—11. Tebb, W. *Leprosy and Vaccination.* London, 1893.

The Final Report of the Royal Commission on Vaccination (London, Eyre and Spottiswoode, 1896) contains an invaluable summary of the history of vaccination and of the evidence laid before the Commission. A volume containing this report, and much information concerning vaccinal complications, will shortly be issued by the New Sydenham Society (Lewis and Co.)

T. D. A.

PATHOLOGY OF VACCINIA

What is vaccinia ?—It is, in the human subject, a specific disorder characterised by the appearance of a local eruption passing through the stages of papule, vesicle, and pustule, associated with more or less constitutional disturbance.

These symptoms are produced, indifferently, by the inoculation of lymph derived from vesicles similarly brought about in a previous case in the human being, or from the eruptive vesicles of a disease of bovine animals called cow-pox. Such inoculation process, whichever way induced, is known as vaccination. This name was originally devised by Dunning, inspired doubtless by the terminology of Jenner, who wrote of the disorder under the title of Variolæ vaccinæ. In this manner Jenner gave expression to his belief that the malady commonly known as cow-pox was in reality nothing more or less than small-pox of the cow.

But soon it was discovered that if there were such a malady as "small-pox of the cow," there was also a small-pox of the horse, which, under the name of "grease," was resorted to as a source of vaccine lymph. Dr. Loy was the first to distinguish, in any satisfactory fashion, constitutional grease from a merely local affection; and thus he explained the failure on the part of many experimenters to transmit horse-pox to the cow.

That a constitutional disease of the horse characterised by a vesicular eruption can be induced by the inoculation of this animal with the virus of cow-pox or vaccinia, has been shown experimentally by Chauveau, who injected vaccine lymph subcutaneously and also into the lymphatics and blood-vessels of colts. In nearly half the number of cases operated on the injection of the lymph was followed by a generalised eruption which Chauveau called "horse-pox." In all probability Jenner was mistaken in his assumption that "grease," in the sense of horse-pox, was a necessary antecedent to cow-pox; but at the same time there can be little doubt that these two diseases are very closely allied, if indeed they be not identical.

That this is so is shown by the fact that numerous strains of vaccine lymph have, from time to time, been raised from the equine source—the protective power of which against small-pox we have reason to believe was equal to that of lymph of undoubted bovine origin. As, however, it is obvious that cow-pox was the source of the lymph stocks first introduced into use by Jenner and his contemporaries, it will be of interest to study briefly the nature and clinical appearances of this disease as seen in the cow and also in man; whether accidentally contracted or intentionally inoculated.

Cow-pox in the cow.—For a description of cow-pox in typical form, as it was known to Jenner and his contemporaries, it is necessary to consult the writings of the early part of the century, at which period the attention of the medical and scientific world had been specially directed to this affection of cows by the teaching of the apostle of vaccination. Probably the most trustworthy accounts are those published by Bryce of Edinburgh, and later by Ceely; and it is from their statements that the following description of the malady is derived.

According to these observers this affection, when once set agoing in a herd, tends to spread with considerable rapidity, the "matter" of the vesicles being carried by the hands of the milkers from one cow to another. It makes its appearance especially in the spring season, and is observed upon the udders and teats of the cows; at first in the form of small vesicles containing a limpid fluid. These vesicles are of a bluish or livid colour, and are surrounded with considerable erysipelatoid swelling and inflammation. If ruptured the vesicles tend to become irregular about the edges; and, unless care be then taken, are very apt to degenerate into foul and troublesome sores. During the course of the affection the cow is not infrequently observed to be in bad health; the appetite is impaired, the temperature is above normal, and the secretion of milk may be considerably diminished. If the material from the vesicles on the udders or teats of the cows happen to come in contact with an abrasion of the skin of the milker's hand, such person is apt to become infected with the disease. When the ailment is communicated in this manner it is termed *casual cow-pox* to distinguish it from that form which is intentionally propagated by inoculation, under which conditions the affection is less virulent than when communicated in the former way. Probably the more severe form in which casual cow-pox usually appears is to some extent due to the situation of the resulting vesicles, and to the purulent nature of the secretion from the sores on the cows' teats or udders.

Casual cow-pox in man.—When cow-pox has been communicated to the milkers in the casual way, small inflamed spots appear in a few days upon the hands, more particularly about the joints and tips of the fingers. These spots quickly assume the appearance of small blisters, somewhat resembling those from burns, which go on increasing until they become large vesicles of a circular form, with a flat or rather a concave surface; their edges being considerably elevated above their centre. They have then acquired a somewhat bluish colour and are found to contain a limpid fluid. After some days the parts around the base of these vesicles become considerably swollen, hard, and inflamed; and, as the affection advances, they may assume somewhat of an erysipelatous appearance. Pain and some degree of swelling of the axillary glands now denote an absorption by way of the lymphatics, and, with the usual symptoms of fever, mark a constitutional affection which is sometimes so severe as to incapacitate the person from following his usual employment for some days. It does not appear, however, that a general eruption ever follows even on the smartest attack of casual cow-pox. After a few days the pain, inflammation, and hardness of the surrounding parts gradually abate; but the vesicles not infrequently ulcerate instead of becoming encrusted and drying up. These ulcerations, however, gradually heal up in course of time without occasioning any lasting injury; and the constitutional affection, although severe, is always transient and unattended with danger: there is no case on record in which casual cow-pox is known to have proved fatal.

Inoculated cow-pox in man.—In the cow-pox induced by inoculation the appearances which present themselves may differ considerably, in some respects, from those which have been described as occurring in the casual disease.

Thus about the third day after the insertion of the virus of cow-pox, either by puncture or by slight incision in the arm, a small inflamed spot may be observed at the point where the inoculation was performed.

Next day this spot appears still more florid; and, on passing the point of the finger over it, a certain degree of hardness and swelling is readily perceptible.

By the fifth day a small pale vesicle occupies the spot where the inflammation began; and the affection begins to assume the characteristic appearance of cow-pox. The vesicle has now a milky-white colour without any inflammatory zone around it, it is evidently depressed in the centre, and its edges are considerably elevated.

For the next two days the vesicle increases in size and retains the same character, so that by the seventh day it has acquired very considerable magnitude; if the inoculation be performed by a puncture, it assumes a circular form; if done by an incision, an oblong form. But in both cases the margin is regular and well defined; while, the centre becoming still more depressed and the edges becoming more turgid, the whole puts on an appearance which is very characteristic of this particular affection.

About the eighth day from the time of inoculation an inflammatory zone begins to appear around the base of the vesicle. This increases for two or perhaps three days more, by which time it may be two inches or longer in diameter and of a bright red colour. At this period, also, the vesicle still retains its concave appearance; the crust in the centre has considerably increased in size, and begins to assume a dark or brownish colour.

About the eleventh day the vesicle has attained its greatest magnitude, and the surrounding inflammation begins to abate. The fluid in the vesicle, which before was thin and transparent, is now more viscid and slightly turbid. After this period the whole becomes quickly converted into a smooth, shining, and somewhat translucent dry crust of a dark brownish or red colour.

This crust, unless forcibly removed, will adhere for a week or more and then fall off, leaving the skin beneath apparently sound, but livid for a time, and more or less permanently scarred.

In children little else than the above local process is noticeable; but in adults constitutional symptoms are apt to be somewhat severe. About the eighth day from the time of inoculation the glands in the axilla become a little swollen, and there is pain and stiffness on moving the arm. Headache, shivering, a rapid pulse, and other febrile symptoms present themselves; and these may persist for a period varying from a few hours to two or more days.

The relationship of variola and vaccinia.—Almost from Jenner's day the value of the practice of vaccination has by some been impugned on the plea that inoculation of one disease—"cow-pox"—could not be expected to exert any really protective action against the disease of small-pox, supposed to be totally different. And, if the thesis of essential difference between these maladies were capable of demonstration, no doubt the objection would be of considerable weight. For there exists little well-authenticated evidence, if any, that the living virus of one disease is capable, when inoculated into an animal, of affording protection against the effects of inoculation of the virus of another and totally different disease; although, no doubt, when two different viruses are inoculated at nearly one and the same time the incubation period of the second infection may be somewhat prolonged. In his first paper Jenner, as has been said, advanced the thesis that small-pox and cow-pox are identical: but, even at the present day, controversy wages hotly around this question; and it still awaits a definite solution.

There can, however, be no objection to our speaking of vaccinia as "one with small-pox"; since it matters little, from our present point of view, whether small-pox, on its transference from man to the bovine animal, becomes actually transformed, or, as some would maintain, merely modified.

During the long period which has now elapsed since the introduction of vaccination, many observers have set themselves the task of attempting, by experimental methods, to solve the problem of the true relationship of variola to vaccinia.

These attempts have all been directed to the possibility of giving rise to cow-pox by the introduction, in one or another manner, of the matter of small-pox into the system of the bovine animal. In the great majority of such attempts, which are vastly more numerous than is generally supposed, the results have been altogether negative. Such has been the case, for the most part, not only in the experiments of Sonderland, Ceely, Chauveau, and others, who endeavoured to introduce the contagion through absorption by the respiratory or circulatory organs, but also in the still greater number of attempts to bring about infection of the system by means of inoculation on the skin. In certain instances, however, these inoculation experiments have been attended by results which, as shown in the Report of the Royal Commission on Vaccination, fall into one or other of three categories:—

The first category includes the experiments in which the inoculation of small-pox matter into the udder, or adjoining parts, of the bovine animal gave rise, at or near the seat of inoculation, to a vesicle, either identical in visible characters with the ordinary vaccine vesicle produced by inoculation with the matter of cow-pox, or to a vesicle the features of which, while not corresponding wholly with those of a perfect vaccine vesicle, so closely resembled it as to justify the recognition of the vesicle as a vaccine vesicle.

Also it includes experiments in which, though the local result had not the characters of a perfect vaccine vesicle, yet lymph from it, when carried through a second or third remove in the cow or calf, presented results fully manifesting those characters; and when again transferred to man gave results undistinguishable from the ordinary vaccine vesicle. Indeed, lymph of such a pedigree has come into general use for vaccination purposes.

Of these experiments, the best known and most quoted are those of Thiele (1838), Ceely (1840), Badcock (between 1840 and 1860), Voigt (1881), Haccius and Eternod (1890), King (1891), Simpson (1892), and Hime (1892); but there are several other experimenters. The details of the experiments are very scanty in the cases of Thiele and Badcock; but more full in the others, especially perhaps in those of Ceely and Haccius.

In *the second category* may be placed the experiments of Klein and Copeman. Klein, who in 1879 had obtained in thirty-one trials what then appeared mere negative results, found in a renewed research in 1892 that the result of the first inoculation in the calf of small-pox matter was not a distinct vesicle, but merely a thickening and redness of the wound. Lymph pressed from the thickened wound, when inoculated into a second calf, produced a like but rather more marked result; while the thickening and reddening still further increased as the process was repeated in a third and in a fourth calf. Lymph squeezed from the wounds of a fourth calf produced in a child typical vaccinia, and crusts from the child produced in turn typical vaccinia in a calf. I myself obtained somewhat similar results; the appearances increased in three removes and approached those of typical vaccinia, but did not reach them.

The third category consists of the results obtained in an elaborate inquiry conducted by a Commission of the Society of Medical Sciences at Lyons, with Chauveau at its head. These results, reported in 1865, were briefly as follows:—Inoculation of the cow or heifer with small-pox matter in any one of the thirty animals used did not give rise to a vaccine vesicle: nevertheless a definite result was obtained, in the form, however, not of a vesicle, but of a thickening and inflammation of the wound; when a puncture had been made this became a papule: lymph squeezed from such a papule, and inserted into a second animal, gave rise to a like papule; and this again might be used for a third animal, but often failed; and the effect could in no case be carried on through more than three or four removes. When the inoculation was repeated on an animal on which a previous inoculation had produced such a papule, no distinct papule was formed; and, moreover, lymph squeezed from the seat of the latter inoculation produced no effect at all when used for the subsequent inoculation of another animal.

There is evidence that the development of the papule was the result of the specific action of the virus. This inference is strengthened by the fact that no such papule was produced by the Lyons Commission when the small-pox matter was inserted into an animal which had previously had cow-pox naturally or artificially; as well as by the fact that when an attempt was made to vaccinate, with vaccine lymph of proved efficacy, an animal on which a papule had been so developed by inoculation with small-pox matter, the vaccination failed; though the animal had never had natural cow-pox nor been vaccinated.

The specific nature of the lymph of the "Lyons" papule is held to be shown by the fact that such lymph, when used on the human subject, gave rise to small-pox. On the other hand, it has been urged that in this case the virus producing the effect was simply the original small-pox matter used in the inoculation, producing the papule and still clinging to the wound. This, however, is considered to be disproved by the experience that lymph from a "Lyons" papule of the second remove also gave rise in the human subject to small-pox. Thus Chauveau and his Commission found that small-pox implanted in the bovine animal gave rise to a specific effect which was not cow-pox, but was of the nature of small-pox; though its manifestations in the cow were different from those of small-pox in man.

With the exception, then, of Chauveau and his colleagues of the Lyons Commission, all the observers mentioned claim to have obtained positive results—in a certain number of their experiments, at any rate—as regards the production of typical vaccinia, after one or more removes, as the result of variolation of the calf.

By no one, apparently, has success been attained invariably; but it is among the experiments of the earlier observers especially, who made use, for the most part, of heifers and milch cows, that the largest proportion of abortive attempts are to be met with. Subsequent experience has shown that success is much more likely to be attained if calves be used instead of heifers or cows. In this way, perhaps, Chauveau's somewhat anomalous results may be in part explained.

With reference to recent experiments on variolation of the calf, it is worthy of note also that, as previously mentioned, different observers have obtained local effects in that animal which, in different calves of a series, have varied considerably. The final result has, however, after a greater or less number of removes from calf to calf, been invariably the same; namely, a local vesicle is produced which, by no means at our command, such as the appearance and course thereof, or the protective power of the lymph derived therefrom, is distinguishable from true vaccinia.

Although practically there is unanimity of opinion among those who have worked at this subject, it must be confessed that, seeing the conditions under which they were carried out, many of the earlier experiments are of little worth. Some of the main objections are based on the use, frequently concomitant, of vaccine and of variolous lymph on the same animal; and on the want of care as to the cleanliness and freedom from vaccine contamination of lancets and "points" used in the experiments.

Objection of similar sort against the variolations of the calf which have been achieved in recent years is hardly valid. In some of the more recent cases, at least, special precautions have been taken to ensure that the instruments and table were sterilised, and to render the environment of the animal such as to afford no likelihood of the communication of vaccinia.

The number of successful cases which have been recorded is now so large, that it is difficult to believe that sources of fallacy of the above sort should have been present in every instance; and it is therefore well-nigh impossible to resist the conclusion that a change of small-pox into vaccinia must really have come about.

If then it can be conclusively proved that small-pox lymph, by passing through the system of the calf, can be so altered in character as to become deprived of its power of causing a generalised eruption, while inducing at the site of inoculation a vesicle undistinguishable from a typical vaccine vesicle; and more important still, if it be shown that when transferred again to man, it has by such treatment completely lost its former power to produce a general disease, it may fairly be asserted that cow-pox—or rather, that artificially inoculated form of the disease which we term vaccinia—is nothing more nor less than variola modified by transmission through the bovine animal. Perhaps the most reasonable interpretation of such results may be that small-pox and vaccinia are both of them descended from a common stock—from an ancestor, for instance, which resembled vaccinia far more than it resembled small-pox. It is conceivable, indeed, that the seeming vaccinia, obtained in the calf by inoculation of small-pox matter into that animal, may after all be but a reversion to an antecedent type; and in this connection we may call to mind a fact of universal experience, namely, that vaccinia, however it may have arisen in the past, or is made to appear in the present, exhibits little tendency to "sport" (as, for instance, by manifesting a "generalised eruption") in the direction of small-pox.

Mr. Picton and Dr. Collins, in their addendum to the *Report of the Royal Commission on Vaccination*, lay much stress on the want of "evidence to show that inoculation of the pox of the cow on the human skin has ever produced small-pox."

Variola and vaccinia may, nevertheless, have a common ancestry, since it is not unlikely that variola may have departed widely from the original type, and have gained an exalted virulence by successive reproduction in man under conditions favourable to its propagation and activity. If this evolution of the disease has, in fact, taken place, variola may have suddenly reverted, under greatly changed conditions, to an ancestral type. But the reverse process is not to be expected. It is most unlikely that a less differentiated form, also emanating from the common ancestral stock, should attain to the most exalted virulence in a single individual, and *per saltum* declare itself as small-pox, as the dissentient Commissioners insist that it ought to do.

Bacteriology of vaccinia and variola.—We owe the first step towards the elucidation of the micro-pathology of vaccinia to Chauveau and to Burdon Sanderson, who by means of filtration and deposit experiments demonstrated, almost concurrently, that vaccine lymph, when freed from its contained particles and inoculated on a living animal, no longer causes vaccinia; while, on the other hand, the precipitate or deposit when employed in similar fashion remains capable of producing the disease.

In consequence, numerous bacteriologists have since devoted themselves to the search in vaccine lymph for a micro-organism to which the special and peculiar effect resulting on the inoculation of such lymph is due.

Among the earlier observers—who, though they cannot be considered to have succeeded in their search for an organism specific to either vaccinia or variola, have yet, by a vast amount of patient research, done much to clear the ground for their successors—may be mentioned Keber, Burdon Sanderson, Klebs, Cohn, Quist, Buist, Carmichael, and Pfeiffer; the names being here set out in accordance with the dates of publication of the results of their work.

The first account of the discovery of micro-organisms in vaccine and in small-pox lymph was that given by Keber of Dantzig, who evidently regarded the bodies found by him as being the carriers (if not the actual generators) of the specific elements of these diseases. Within the next two years the occurrence of similar bodies in vaccine lymph was described by Burdon Sanderson and by Klebs.

In 1872 an important paper was published by Cohn of Breslau in which he treated the morphological aspects of the subject with much completeness. His observations, which related both to vaccine and variolous lymph, have, at least as regards the lymph obtained from mature vesicles, received entire corroboration from all subsequent workers; with this exception, however, that while he apparently believed the micro-organisms found by him to be of one species only, to which, accordingly, he gave the name micrococcus vacciniæ or variolæ, as the case might be, later observers have shown that microbes of more than one species are usually to be found in any given specimen of lymph.

Cohn called attention to the fact that in perfectly fresh vaccine lymph the "corpuscles" for the most part occur singly, others being joined together in pairs in a form resembling the figure 8; and he states that after the preparation has been kept for a time, the number of "these double cells increases, and that soon chains of four begin to be distinguishable. These chains are usually curved or in zigzags; their attachment one to another is evidently very slight, as they can readily be displaced. . . . After a few hours' observation they are seen to be all aggregated into irregular colonies or clumps, each consisting of sixteen, thirty-two, or more corpuscles." He also noted a point of importance in connection with the opacity which is apt to occur in stored lymph; namely, that "in capillary glass tubes the multiplication of colonies sometimes lasts a long time, so that they acquire considerable size, and present themselves as flocculi."

About ten years later Quist published a series of experiments dealing with the cultivation of the micro-organisms present in vaccine lymph in media outside the animal body. He obtained the best results with a culture fluid composed of equal parts of blood-serum, glycerine, and distilled water, which he rendered alkaline by the addition of one part in three hundred of carbonate of potash. After sterilising this fluid by exposing it to a temperature of 60° C. for an hour and a half on three successive occasions, it was inoculated with a minute piece of sterilised sponge soaked in clear lymph, or with a piece of vaccine "crust" which had been washed in distilled water, and then carefully dried. Quist found that growth eventually occurred both on and below the surface; the former consisting of minute floating scales, while the latter gradually settled to the bottom of the vessel as a fine sediment. The scales, forming a scum on the surface of the fluid, he found to be composed of swarms of micrococci which, when inoculated into the skin of animals, gave rise in some cases to what he regarded as a typical eruption of vaccinia. He does not, however, appear to have been successful with subcultures. Still he showed, as did Müller also, that the specific contagium of vaccinia could exist, for a time at any rate, in a fluid composed in part of dilute glycerine; and it was probably in consequence of their work that this substance has come much into use in the storage of vaccine lymph.

Among the most extensive and laborious series of experiments dealing with the isolation of the various micro-organisms found in vaccine and in variolous lymph are those detailed by Buist of Edinburgh. His experiments resulted in the separation of three different species of micrococci which, when grown on the ordinary nutrient media, gave rise to cultivations of a white, yellow, and orange colour. All these three Buist appears to have regarded as essential constituents of vaccine lymph, for he speaks of them as white, yellow, and orange vaccine respectively. From specimens of variolous lymph he succeeded in obtaining one organism only, the colour of which, when grown on solid media, was white. With none of these cultures did he obtain any definite result on the inoculation of calves, monkeys or man.

It was reserved for Pfeiffer to show that the various micro-organisms isolated by his predecessors, although constantly to be found in lymph, were identical with certain definite species with which he was familiar in various tissues and body fluids under circumstances which had no relation either to vaccinia or variola.

If this were so, none of these organisms could be regarded as concerned in the specific action of the lymph.

Crookshank, also, in his evidence before the Royal Commission on Vaccination, and again in a paper communicated to the International Congress of Hygiene in 1891, stated that he has succeeded by the method of plate cultivations in isolating from vaccine lymph an immense number of bacteria; of these he set out a detailed list. But he makes no statement of the precautions, if any, which he took in the collection of the lymph; neither does he attempt to distinguish between those bacteria which are commonly to be found in lymph and those the presence of which is exceptional.

As the result of my own work it appears that three species of micro-organisms; namely, Staphylococcus albus epidermidis, S. pyogenes aureus, and S. cereus flavus,—corresponding probably to Buist's white, orange, and yellow vaccine respectively—are one or more of them to be found almost universally in specimens of vaccine lymph; of these the Staphylococcus albus epidermidis is usually to be found in the upper layers of healthy skin. The Streptococcus pyogenes is also present in lymph occasionally.

More recently, however, Klein and myself, working independently, have found it possible, by the use of certain staining methods, to demonstrate both in vaccine and in variolous lymph the presence of a small, short, almost oval, spore-bearing (?) bacillus; sometimes in considerable numbers. This bacillus, which has also been observed by Kent and myself in sections of skin passing through the site of a vaccine vesicle obtained from a calf, is to be found most readily in early lymph; in lymph, that is, taken on the fourth or fifth day (seventy-two to ninety-six hours) in the calf, and in the human vaccine (or variolous) vesicle about the fifth day of eruption; while later lymph, such as that obtained from the human subject at the ordinary period for purposes of vaccination, contains but a few at the most. This fact, which not improbably has relation to spore formation by the bacilli about the time of maturity of the vesicle—together perhaps with overshadowing of them by extraneous organisms at the later stages—probably accounts for their presence having been overlooked hitherto.

If proper precautions as to time and method be taken in the collection and subsequent staining of the specimens of early lymph, it is usually found that, although these bacilli are present often in extraordinary numbers, other bacteria are conspicuous by their absence.

The fact that these apparently identical bacilli are to be found both in vaccine and in variolous lymph of about the fifth day of eruption, tends to support the hypothesis that they constitute the active contagium of the diseases in question; and the further fact that it has not been found practicable to cultivate them in any of the artificial media ordinarily employed, renders it well-nigh certain that they are not merely "extraneous" saprophytic organisms.

Although not capable of growth on gelatine, agar, serum, and so forth, I have succeeded in obtaining cultivations of the bacillus found in variola by employing for the purpose the hen's egg, inoculated with an emulsion of small-pox crusts in normal saline solution or dilute glycerine, and incubated for about a month at the body temperature.[1]

Psorosperms or sporozoa in lymph.—In consequence, no doubt, of the apparent impossibility which existed until recently of isolating any bacterium from vaccine lymph which could be regarded as peculiar to vaccinia, several observers have sought to prove that organisms of a somewhat higher order than bacteria might be concerned in the production of this malady, and also of variola. For instance, bodies believed to be of the nature of psorosperms or sporozoa have been described in and among the epithelial cells of an inoculated area by Pfeiffer, Guarnieri, Monti, Van der Loeff, Doehle, and Sicherer on the Continent, and by Ruffer and Jackson Clarke in this country.

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[1] Since this was written, pure cultures of these microbes have been obtained on artificial media from both small-pox and vaccine lymph and crusts. The growth for the first few removes, at any rate, though abundant, is practically invisible to the unaided eye.

Ruffer and Plimmer describe the alleged parasite as a small round body which sometimes appears to have a more darkly staining centre. It is, they say, about four times the size of an ordinary staphylococcus, and generally lies in a clear vacuole in the protoplasm of the epithelial cells of the stratum Malpighii, and occasionally indents the nucleus, though it has not been found enclosed in the latter body. These observers state that they have found the same organisms in sections of skin from small-pox patients and in small-pox pustules of the larynx and trachea.

Pfeiffer describes similar bodies, not only in the epithelial cells of the vaccine vesicle, but likewise in all other vesicular eruptions of man and the lower animals. Pfeiffer, Guarnieri, Ruffer, and Plimmer all assert that these parasites exhibit very slow amœboid movements.

There can be no doubt, of course, as to the occurrence of the appearances described, although we may not be prepared to accept the interpretation put upon them; and in this connection it is well to bear in mind not only that the bodies enclosed in cells described by Guarnieri, Monti, and Ruffer are said by them to differ essentially in their staining reaction and in their appearance from those of Pfeiffer, Van der Loeff, and others, but also that the most recent experimental work in this direction has been carried out on the cornea of the rabbit, an animal which there is reason to believe is insusceptible to vaccinia.

It may be added also that no such bodies have been satisfactorily demonstrated in vaccine lymph itself. It is therefore conceivable that the "parasites" in question may represent merely the result of epithelial irritation caused by the scarification, together with that—of a non-specific nature, however—set up by the vaccine lymph employed.

A Small-pox antitoxin.—Inspired by the investigations of Tizzoni and Cattani on tetanus, and, later, of Behring on diphtheria, attention has been directed for some time past to the production, if possible, of an antitoxic serum, which might be of use in the treatment of small-pox, for when once this disease is fully manifested vaccination is practically of no avail. The results of experiments in this direction recorded by different observers are, however, somewhat conflicting.

Thus Kramer and Boyce were unable to produce any immunity even with large doses of serum from vaccinated calves; and recently Beumer and Peiper have arrived at a similar conclusion. On the other hand, Kinyoun, and Hlava and Houl claim successful results; but, so far as can be judged from their publications, such claim would appear to rest on somewhat slender foundation; although Hlava and Houl state that in one instance the injection of their serum to the extent of 0·6 to 1·0 c.c. per kilo of body-weight of the experimental calf entirely prevented the action of vaccine lymph inoculated four days later. They have not as yet put on record any experiment with variola.

The fullest and most recent contribution to this subject is that of Béclère, Chambon and Ménard. The conclusion at which these authors arrive is that the serum of a vaccinated heifer, gathered after the drying of the pustules, immunises to a certain extent against the effects of subsequent vaccination; but the diagrams with which the paper is illustrated show that the antagonism is by no means complete.

History of various lymph stocks.—Jenner's first case of vaccination was that of a boy, eight years of age, whom he inoculated in the arm with cow-pox matter taken from a sore on the hand of a dairymaid who, in turn, had become infected with the disease from milking cows suffering from cow-pox.

This was in 1796; but it was apparently not until two years later, in 1798, that he made his first attempt to carry on a strain of lymph from arm to arm. In the spring of this year he inoculated a child with matter taken directly from the nipple of a cow; and from the resulting vesicle on the arm of this child first operated on, he inoculated, or, as it may now be more correctly termed, "vaccinated" another. From this child several others were vaccinated; from one of these a fourth remove was carried out successfully, and finally a fifth. Four of the children were subsequently inoculated with small-pox—the "variolous test"—without result.

At this point, however, the strain appears to have been allowed to die out; but, in January 1799, Woodville, one of the physicians to the Small-pox Hospital in London, who had been much interested in Jenner's investigations, discovered the presence of cow-pox in a dairy in Gray's Inn Lane. With lymph obtained from one of the cows in this dairy, he vaccinated seven persons at the Small-pox Hospital; while in the case of certain other persons he employed matter from sores on the hand of a dairymaid who had become infected from one of the cows at this same place. These cases, from which afterwards in succession many hundreds of persons were vaccinated, were the source of what is usually spoken of as "Woodville's lymph."

These strains of lymph were extensively distributed both by Woodville and also by Pearson, one of the Surgeons to St. George's Hospital; but even at this period lymph from several other sources had also come into use.

Thus Pearson very early obtained lymph from a dairy in the Marylebone Road and elsewhere; while Jenner who, having for a time no supply of his own, had used some of Woodville's hospital lymph, obtained a further supply from a cow at a Mr. Clarke's farm in Kentish Town.

The lymph first employed on the Continent and in other foreign countries was undoubtedly supplied in large measure by Pearson and Woodville; although we learn from Baron and other authors that Jenner, who was naturally much appealed to for supplies of lymph, himself sent lymph to Stromeyer of Hanover, to De Carro of Vienna, to Berlin, and to Newfoundland.

Strains derived from lymph stocks originally supplied by Jenner were also sent abroad by various persons; the original strain being, in large measure at any rate, the lymph obtained by Jenner from the Clarke's Farm cow. It would be erroneous to suppose, however, that all the lymph employed abroad in the early days of vaccination was obtained from England. Indeed both Sacco and De Carro made extensive use of lymph obtained by the former from a case of natural cow-pox which he discovered in

Lombardy. From this stock also De Carro sent supplies to Constantinople, where it was employed for the first vaccination carried out in this part of Europe. De Carro it was also who first succeeded in conveying a supply of lymph to India. This lymph, again, was not from Jenner's stock, but was of Milanese origin, having been furnished to him by Sacco. It was, moreover, not of bovine, but of equine origin, and, according to De Carro, had never been passed through the cow.

Among more recent strains may be mentioned that obtained in 1836 at Passy, in the environs of Paris, from the hand of a milker who had contracted casual cow-pox.

The old stock then in use at the Académie de Médecine had evidently degenerated somewhat; and, when its effects were compared with those of the new Passy lymph, the vesicles developed from the latter were found to be manifestly finer.

In 1836 Estlin of Bristol put in circulation a stock which at first showed unusual activity. This abated, however, after some transmissions, and the lymph afterwards came into extensive use.

From this time onwards the various stocks became so numerous that Ceely, writing in 1841, states that during the preceding three years he had experimented with lymph from more than fifteen distinct sources; of these six had been taken from the natural disease, either direct from cows or from vesicles on the hands of the milkers, and seven were artificially produced in the cow.

The lymph stock in use at the present time at the Government Animal Vaccine Establishment was originally obtained on 26th November 1881 at a farm in the village of Lafôret, not far from Bordeaux; whence a sample of lymph from the seventeenth calf in succession from the animal first affected was sent by Dr. Dubreuilh, of Bordeaux, to the Medical Officer of the Local Government Board.

Of late years, more particularly, numerous strains of so-called variola-vaccine lymph, obtained by inoculation of human small-pox on the calf, have been introduced especially by Fischer, by Haccius, and by King, and have been transmitted through many thousands of individuals.

In discussing the origin of the various lymph strains at present in use Messrs. Collins and Picton, in their addendum to the *Report of the Royal Commission on Vaccination*, make a point of the impossibility of employing the "variolous test" as a proof of the efficacy or the reverse of any particular lymph stock.

It is, indeed, a penal offence at the present time to inoculate a human being with variola, but to demonstrate that it is, nevertheless, by no means impossible to test the potency of any given sample of lymph by this method, mention may be made of certain experiments carried out by myself with the object of determining this question. Monkeys were employed, on account of their similarity in many respects to man; and it was found on experimental investigation that they are susceptible both to vaccinia and variola.

In the cases of variola and of vaccinia alike the local result of inoculation attains its acme (*qua* vesiculation) in the monkey, as in the human being, about the eighth day. The first signs of reaction appear usually on the third day, by which time, if variolous lymph has been used, there is a distinct though very thin crust over the site of inoculation. The chief difference noted between the effects resulting from the local inoculation of these two diseases in the monkey is, that in the case of variola there is more or less of a crust from the first; that vesiculation is less marked than in vaccination; that about the ninth to the eleventh day a general eruption may appear, which, in some instances, covers the whole surface of the body, and that the final scab at the site of inoculation is not so elevated in the variolated as in the vaccinated animal.

Proof having been thus obtained that this animal is capable of being infected both with vaccinia and variola, and that it passes through these diseases in forms similar to those witnessed in man, it was determined to make trial of the protection against small-pox afforded in the monkey by previous vaccination, and of the protection against vaccination afforded it by variolation; and it appeared desirable also to compare the effect produced by the use of human and of calf vaccine respectively.

For this purpose humanised lymph was obtained from Birmingham, where it is stated that the same strain of lymph has been continuously carried on by means of arm-to-arm vaccination for the past thirty-eight years; the calf lymph was obtained from the Government Animal Vaccination Station in Lamb's, Conduit Street, and small-pox lymph was supplied from the hospital ships in the Thames, from Warrington, and from Manchester. As the result of many experiments extending over a period of several months, it became obvious that the mutually protective power of lymph obtained from these three different sources when inoculated on the monkey, is practically identical in all respects; the second inoculation having invariably been productive only of a negative result.

The criticism of Messrs. Picton and Collins, therefore, falls to the ground; since if it is desired to apply the "variolous test" to any given lymph stock, all that is necessary is to vaccinate a monkey with a sample of the lymph in question, and subsequently to inoculate the animal with potent small-pox lymph after the lapse of such period from the first operation as may be thought proper.

Morphology and chemistry of vaccine lymph.—Fresh vaccine lymph, taken before full maturity of the vesicle, is a clear, transparent, limpid fluid, almost colourless in man and slightly straw-coloured when obtained from the calf; this difference in colour depends on the varying quality of the normal pigment present in the blood plasma. Calf vaccine lymph is also somewhat more viscid than human lymph, and does not flow so readily when the vesicle is punctured; thus it is usually necessary to use compression forceps in the collection of calf lymph. Examined microscopically, vaccine lymph contains a certain amount of epithelial débris; a few cells and portions of cells being always visible. Leucocytes are usually present also, the number depending on the stage at which the lymph is taken; few or even none are to be found in the contents of the vesicle when first formed, but at or after the period of maturation they may be so numerous as to render the lymph turbid, or even puriform.

A few red blood corpuscles may be noticeable, although most observers will hardly agree with the statement made by Dr. Husband to the Royal Commission on Vaccination that this is invariably the case.

In stained specimens, particularly, micro-organisms of one or more varieties can, as I have said, readily be demonstrated ; the actual numbers being dependent to a certain extent on the care with which the lymph has been collected.

The nature and significance of the various microbes which at one time or another have been isolated from specimens of vaccine lymph has been discussed in the section on Bacteriology (p. 642). It is matter of common knowledge that lymph, when stored in capillary tubes, tends after a longer or shorter interval to become cloudy, under which circumstances it is also liable to be uncertain in its action when subsequently used for the operation of vaccination.

This opaque appearance may be quite independent of any coagulation of the lymph, as may not infrequently be demonstrated on breaking tubes in which it is most marked. On the other hand, where clotting has taken place after the lymph has been stored, the opacity tends to form with the coagulum a central whitish thread in the midst of a clear fluid ; instead of being distributed through the lymph in discrete points as may otherwise be the case.

If cultivation experiments be carried out by inoculation on nutrient media, the number of colonies resulting from such inoculation with the contents of tubes which have become opaque is usually much greater than if fresh lymph is employed in a similar manner. We are apparently justified, therefore, in considering that the opacity of old stored lymph is, in the main, the outcome of an enormous multiplication of aerobic bacteria, the ancestors of which are present in the lymph when first collected ; although their numbers are then so comparatively small as not to render it in any way turbid. It follows that vaccine lymph which has become opaque should never be employed for vaccination.

Vaccination lymph, chemically speaking, consists of the serum, or rather of the plasma of the blood. When freshly obtained, therefore, it is faintly alkaline in reaction ; but it becomes distinctly acid after a time when stored. In addition to the various salts and proteids normally present in the blood-plasma, vaccine lymph contains some substance, possibly of the nature of a ptomaine, which results from the vital activity of the specific organism peculiar to vaccinia. That this is so may be proved either by filtration of the lymph through porcelain or by exposure of it to a temperature of about 50° C. If such filtered or sterilised lymph be inoculated on the skin in the usual manner, no obvious effect is produced at the point of inoculation ; but it will be found that the animal has been rendered temporarily immune to the effects of subsequent vaccination with lymph of normal potency.

Histology of the vaccine vesicles.—The histology of the vaccine vesicle has been experimentally studied in the calf by Stanley Kent.

He finds that some hours after inoculation considerable inflammatory disturbance takes place, the cells poured out, together with the fibrinous exudation, forming a plug which completely occludes the inoculation wound. In the plug are numerous colonies of micrococci; but very few organisms make their way into the surrounding tissues. The blood-vessels in the neighbourhood are engorged with blood, and there is an outflow of leucocytes towards the point of injury.

The blood-vessels also contain numbers of organisms which there is reason to suppose are the actual material of the disease. These organisms are very minute (1 m. in length and 0·5 m. in thickness) and commonly occur as groups of two individuals placed end to end, thus forming what may be called *diplo-bacilli*. Some of the organisms float freely in the liquor sanguinis; others are contained within cells, some of which enclose groups of ten or twelve organisms, whilst other cells are so loaded that they appear to be simply masses of bacteria. The neighbouring tissues, though free from organisms, seem to respond to the influence of the process, cell-proliferation taking place and the nuclei changing their characters. Close to the incision many cells are completely broken down into angular fragments.

Later, other changes take place; most of the micrococci disappear from the plug; the plug itself becomes larger, and the inflammatory process extends far into the surrounding tissues. Each neighbouring blood-vessel becomes the centre of an aggregation of leucocytes, which are poured out and wander off to swell the crowd already surrounding the area of infection on all sides.

A coagulation necrosis takes place in the cells of the rete Malpighii; and the cells become transformed into a network of trabeculæ, the meshes of which are distended with the fluid exudation. The nuclei of these cells break down and undergo changes which have been fully described elsewhere. The vesicle which arises is multilocular, the separate loculi being distended with fluid which, although at first clear, subsequently becomes cloudy.

By the fifth day the inflammation and infiltration have extended to a considerable distance from the seat of inoculation, and the blood-vessels are surrounded by masses of extravasated leucocytes. The blood-vessels do not contain so many micro-organisms at this stage as in an earlier period; but a little later a great number of cells containing the diplo-bacilli may be found in the tissues at some distance beneath the point of inoculation. These cells, which appear to be leucocytes, are, however, no longer in the vessels, but lie free in the tissues; moreover they do not contain, as formerly, large groups of organisms, but as a rule one or two only.

The *staining* of these micro-organisms is very difficult. The best results are obtained by heating specimens in carbol-methylene blue solution.

Even at the eleventh day cells containing organisms remain fairly numerous. In the later stages the original multilocular vesicle becomes converted into a unilocular pustule by the thinning of the trabeculæ, which finally break; and by the increase in the number of leucocytes. The fluid dries up and, together with the necrosed epidermic cells, takes part in the formation of the crust, which under the microscope appears as a homogeneous mass very deeply coloured by the ordinary stains.

Meanwhile a regeneration goes on underneath the crust, the new epidermis being formed by a growing in of the surrounding stratum Malpighii. The extent to which the cutis vera has been involved determines the depth of the resulting scar.

PRACTICE OF VACCINATION

Collection and storage of vaccine lymph.—Hitherto the use of arm-to-arm human lymph has been insisted on in this country in the case of all vaccinations performed at public stations, for the reason that until recently this was the only method by which lymph stocks could be perpetuated, and the greatest possible purity of the lymph ensured.

In view, however, of the recommendations of the Royal Commission, it is likely that this method will be discontinued in the future in favour of the use of calf lymph, with the object of diminishing the very remote possibility of the conveyance of syphilitic infection by the operation of vaccination (p. 610). By this change of method the Commissioners also consider that the necessity for opening vaccination vesicles, and thereby of affording opportunity for other local infections, would be avoided—such precaution being in their opinion a desirable one, although they add that its importance has been exaggerated.

If human lymph be required, the vesicle should be opened by a number of minute punctures, which must be made on its surface and not around its base. The object of such multiple puncture is to open the various cell-spaces in which the lymph is contained; that of puncturing on the surface rather than around the base is to avoid any admixture with blood. Lymph soon collects in droplets at the points of incision, and may be removed on a lancet; or, if required for use at a distance, may be taken up into capillary tubes. On no account should the vesicle be pressed or squeezed in order to increase the flow of lymph, supposing the amount to be but scanty; and, on the other hand, if it be very thin, and consequently flow too readily, it should not be employed for use in vaccination.

The collection of calf lymph is a matter of rather more difficulty, as owing to its greater degree of viscidity and to the closer texture of the cell-spaces in the vesicle, it does not flow readily when the vesicle is punctured. For this reason it is necessary to employ compression forceps, between the blades of which the vesicle is taken up and confined by means of a catch while the lymph is being removed.

Lymph, whether human or calf, that is not required for immediate use may be preserved either in the dry state on "points"; or in the liquid condition, in capillary tubes which must be hermetically sealed after being filled.

The points used for the dry storage of lymph have hitherto been made of ivory, but it has been suggested that celloidin would be a more suitable substance for the purpose, as a smooth non-absorbent surface would be thus obtainable. They are usually about a couple of inches in length, and pointed at one end.

In order to charge the points they, in this country, are well dipped in the lymph exuding from a vesicle; and when a fair-sized drop has been collected on them, they are placed on some raised and flat surface, such as a plate turned upside down, with their moistened ends over the edge, until the lymph has thoroughly dried.

They should be kept until needed in a clean, well-stoppered bottle. To prepare the lymph for use, a small drop of water is placed on the end of the "point" in order to moisten the dried material. This may now be removed with the point of the vaccinating lancet, or the end of the "point" may be rubbed over scarifications of the skin previously made with a lancet. In the *Report of the Royal Commission on Vaccination*, however, the opinion is expressed that safety would be increased by preserving the lymph in tubes instead of on "dry points."

The capillary tubes employed for the purpose of lymph storage should be similar to those first introduced by Dr. Husband of Edinburgh. In order to fulfil their intended purpose they should be (i.) large enough to contain sufficient lymph for one vaccination; (ii.) long enough to admit of both ends being sealed hermetically without subjecting the charge to the heat of the flame; (iii.) of such tenuity that they can be sealed instantaneously in the flame of a spirit lamp; and (iv.) of such strength as not to break easily in handling. To fill a capillary tube it should be held in a more or less horizontal position, and one end applied to the drop of lymph exuding from a vesicle which has been punctured, when the lymph immediately enters by capillary attraction.

No more should be allowed to enter than is sufficient to fill the tube from one-half to two-thirds of its length. The tube is sealed by applying the empty end to the flame of a candle or spirit lamp, as much as possible of the contained air having been previously driven out by momentarily plunging into the flame the whole of that portion of the tube in which there is no lymph.

By this means, as soon as the extremity is sealed, the column of lymph is driven by atmospheric pressure towards the end first closed; and the point at which the lymph found entrance can then be sealed in the flame in the same manner as was the other.

Glycerinated Lymph.—The practically universal occurrence of extraneous microbes in vaccine lymph and the chance of addition, during or after vaccination, of pathogenetic organisms by agency of careless people, whether vaccinators or persons having charge of infants, have been advanced as reasons for avoiding vaccination, on the grounds of the possible harmfulness of the extraneous organisms liable to be introduced into the lymph at the time of the operation or subsequently in the course of the evolution of the resulting pock.

This argument, however—so far as the microbes usually intimately associated with lymph are concerned — loses whatever weight it may have had, since I have shown that by thoroughly incorporating four parts of a sterilised 50 per cent solution in water of chemically pure glycerine with one part of the lymph or vesicle pulp, and afterwards storing the mixture for some weeks prior to use in sealed capillary glass tubes, protected from light, all the ordinary saprophytes found associated with lymph are eventually destroyed. This result is proved by the fact that no growth arises in any of the ordinary culture media inoculated with such glycerinated lymph. This statement applies equally to the bacillus of tubercle and to the streptococcus of erysipelas, which have been added experimentally to vaccine lymph.

In glycerinated calf lymph properly produced we have then a preparation which, while even more efficient as vaccine than the original lymph, can be produced entirely free from the "extraneous" organisms which, at one time or another, have been isolated from fresh or stored lymph; with the possible solitary exception, in the case of lymph obtained from the calf, of bacillus subtilis—the common hay bacillus—which, however, possesses no pathogenetic properties.

This statement, since the first publication in 1891 of the experiments on which it is based, has received ample corroboration from many other observers, among whom may be mentioned Chambon, Ménard and Straus, Leoni, Kinyoun, and Klein.

There can be little doubt, therefore, of the superiority of the suggested method of lymph storage over the perhaps simpler methods which up to the present have been commonly employed in England. In Germany, Belgium, and elsewhere, for some time past, and for various reasons, admixture with glycerine has been made use of in the preparation and storage of vaccine material; but hitherto apparently without knowledge of the peculiar action exerted by such treatment in the purification of lymph. Kitasato, indeed, has recently published a series of experiments in which he sought to free vaccine lymph from extraneous bacteria by the addition of carbolic acid to the extent of 0·5 per cent to 8·66 per cent. He states that in each case the carbolic acid was added to samples of trade lymph which had, however, already been diluted, in the process of preparation, with a mixture of glycerine and water.

In the preparation of glycerinated lymph on a large scale the calf, which on the previous day should have been injected with tuberculin in order to ensure that it is not suffering from tuberculosis, is strapped down to a table of special construction, and the abdomen is shaved from the pubes to the umbilicus: occasionally, when a larger surface is required, the inside of the thighs is also shaved. The shaved area is then thoroughly cleansed with soap and hot water, and swabbed with a solution of corrosive sublimate; and this in its turn is washed off with sterilised water. With a somewhat blunt scalpel superficial incisions are then made fairly close together over the whole surface of the shaved portion of the skin, care being taken to remove with a sterilised towel or blotting-paper any traces of blood which may appear. A sufficient quantity of glycerinated lymph must be now thoroughly rubbed over the incisions with the flat portion of the blade of the scalpel; and when this has dried in the calf may be removed from the table and returned to its stall. After the lapse of about ninety-six hours from the first operation, the calf is again placed on the table, and the epithelium and underlying vesicular pulp are removed by means of a steel spoon, firm pressure being employed so as to avoid as far as possible the presence of blood. The scrapings are collected in a Petri dish, or other suitable receptacle, and immediately weighed. To this material is then added four times its weight of a sterilised mixture of 50 per cent of chemically pure glycerine in distilled water; and the whole is thoroughly ground down together. The latter process is carried out either by hand, a small pestle and mortar being employed for the purpose, or, more rapidly and perhaps more efficiently, by means of a mechanical mixing machine.

The resulting mixture, or emulsion as it is sometimes called, which will be sufficient in amount for at least 2000 vaccinations, may be kept in bulk until required for distribution; it must be stored in a cool place and protected from the light. If desirable, however, it may be drawn up at once into capillary tubes, which should be of somewhat larger diameter than those which are commonly employed for the storage of unmixed lymph. If this be done the tubes should be filled about two-thirds full, and the ends then carefully sealed in the flame of a spirit-lamp or Bunsen burner.

Insertion of vaccine lymph.—This process may be carried out either by puncture, by multiple superficial incisions, or by scarification. Doubtless the individual operator will attain the greatest measure of success by employing the method with which he is most familiar; but there can be little doubt that the method of insertion by scarification is the one which is most generally satisfactory. This statement applies not only to the use of fresh lymph, but also to stored lymph, whether on dry points or in tubes; and more particularly if the lymph has been preserved with glycerine.

The mode of operation is briefly as follows:—

The arm should, if possible, first be washed with warm soap and water, and afterwards carefully dried with a soft towel, gentle friction being employed so as to cause a certain amount of distension of the cutaneous capillaries. Drops of lymph, corresponding in number to that of the vesicles which it is required to produce, are then to be placed on the surface of the arm, and the skin put slightly on the stretch with the fingers of the left hand. Next the skin is scarified by a method of cross-hatching through the drops of lymph by means of whatsoever instrument may be preferred, care being taken not to place the insertions too closely together, lest the vitality of the tissues between them be injured.

An ordinary bleeding lancet, the point of which has been slightly blunted, or a flat-headed surgical needle, are both very efficient for the purpose of scarification; complicated instruments should be avoided since, as a rule, it is difficult to keep them thoroughly clean.

The special advantage of a needle is that a new one can be employed on every occasion; if a lancet or like instrument be employed, it is essential that it should be boiled or otherwise sterilised immediately before use; and, further, that it should be dipped into boiling water and wiped on a piece of sterilised cotton-wool, not only between each operation, but, in the case of arm-to-arm vaccination, in the event of the vaccinator having to return to the vaccinifer for the purpose of obtaining more lymph.

S. Monckton Copeman.

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S. M. C.

VACCINATION AS A BRANCH OF PREVENTIVE MEDICINE

Introductory.—Impartial students of the history of medical progress readily admit that vaccination, which has now stood the test of practice for a century, remains to-day one of the greatest medical prophylactics the world has ever known. Like all other measures for improving the general health of the community, it emanated from and has been fostered by the medical profession; but the assertion so frequently made by ignorant or unscrupulous laymen, that the profession has been influenced in its exertions to maintain the practice by motives of pecuniary benefit is so obviously ungenerous as only to call for passing notice. The number of doctors who derive any substantial benefit from the practice of vaccination is very small; and those who consider that the bulk of medical men are so inordinately mercenary as to lend themselves to the support of a false system for the sake of a few shillings a year, should remember that it is the prevalence of disease, and not its prevention, which best pays the practitioner: a widespread outbreak of small-pox must prove far more remunerative than the small fees to be earned by vaccination. If people would but bear in mind that the sanitary science of which England is to-day so justly proud, and which has led during the last fifty years to a marvellous reduction in the mortality from filth diseases and an increase in the average length of life, owes its origin and development to medical men, they would the more readily understand that had vaccination not possessed the powers claimed for it, the medical profession would have been the first to cast it aside, as they have rejected other false practices.

In spite, however, of the above weighty considerations, we have to face the fact vouched for by the Medical Officer of the Local Government Board, that there is at the present time "a larger amount of default in regard of vaccination than any which has been recorded since the passing of the Vaccination Act of 1871," and "a steadily growing increase in the younger population of persons who are altogether without protection against small-pox." Moreover, it would be ridiculous to ignore the fact that perfunctory vaccination is very much on the increase.

Causes of the present defaults in vaccination.—This falling off in infantile vaccination is, no doubt, largely due to the absence of any widespread epidemic of small-pox throughout the country within recent years; the feeling of false security thus created has led a number of parents to put off for the moment the temporary inconvenience of having their infants vaccinated. As might well be expected under these circumstances, whenever small-pox threatens to spread in a district there is a rush for vaccination amongst the unprotected, which, by straining the local resources to their utmost limits, is not calculated to secure the most efficient protection in all cases. Moreover, experience has shown that with the subsidence of the immediate danger the rule of apathy again sets in.

Influence of Antivaccinators.—But, although individual apathy has had much to do with the falling off in the amount of infantile vaccination, the main portion of the mischief is undoubtedly attributable to the baneful influence of a number of opponents of the system, who persistently disseminate gross misrepresentations calculated to create a distrust of vaccination. Vaccination has fallen into the greatest neglect in those towns in which the leaders of the opposition are most active. It has been truly said that if persons who so readily neglect vaccination at the bidding of a few energetic, but not too scrupulous agitators, could look on the sight, common in every small-pox epidemic, of a family, living together in the same house and under precisely the same conditions, invaded by small-pox, the unvaccinated members developing the disease in all its loathsome virulence, the recently vaccinated or revaccinated escaping altogether, and those who years previously have been vaccinated more or less efficiently escaping with a few spots and slight constitutional disturbance, the perverted statistics and the sophistries of the antivaccinators would be brushed aside for ever, and the apathetic would hasten to secure for themselves and their offspring the protection which vaccination affords.

Small-pox in prevaccination times.—To obtain an adequate notion of the appalling ravages of small-pox in its unfettered activity we have but to look back at its past history. We find that in 1518, for instance, it helped to complete the depopulation of St. Domingo which fire, sword, and famine had begun. Soon afterwards, in Mexico, it even surpassed the cruelties of conquest, suddenly smiting down 3½ millions of population. Prescott, in his *Conquest of Mexico*, describes the epidemic as "sweeping over the land like fire over the prairies, smiting down prince and peasant, and leaving its path strewn with the dead bodies of the natives, who (in the strong language of a contemporary) perished in heaps like cattle stricken with murrain." In Siberia and Kamschatka, in Greenland and Iceland, in Sweden, in Brazil, in Borneo, on the Gold Coast, in Madagascar, its devastations were similar; and striking accounts of its ravages among the North American Indians may be gathered from the following passage in a work by Mr. Catlin published in 1841: "Thirty millions of white men are now scuffling for the goods and luxuries of life over the bones and ashes of twelve millions of red men, six millions of whom have fallen victims to the small-pox, and the remainder to the sword, the bayonet, or whisky." To turn to Europe, we find that during the eighteenth century, in the words of Bernouilli, a trustworthy statistician, "fully two-thirds of all children born were, sooner or later, attacked by small-pox, and that on an average one-twelfth ($\frac{2}{3} \times \frac{1}{8}$) of all children born succumbed to that disease." In England, according to the calculations of Dr. Lettsom, the average annual deaths from small-pox were about 3000 out of every million of population; a death-rate which, on the present population of England, would give an average of nearly 80,000 deaths a year from small-pox. Nearly one-tenth part of all the persons who died in London within the Bills of Mortality during the latter half of last century died of this one cause alone. As on the Continent, so in England, the younger part of the population were peculiarly its victims; and royal and noble families were not exempt.

The ravages of small-pox are not, however, half enumerated in the list of the myriads whom it has killed. From the earliest to the latest records of the disease there is constant mention of the tax which it levied upon survivors. Bernouilli states that "many who did not die were rendered sickly or deformed for life, and diseases of the eyes and blindness often ensued from the scourge"; and Macaulay, who justly assigns to variola the foremost place as "the most terrible of all the ministers of death," exclaims, in an eloquent passage, "The havoc of the plague had been far more rapid: but the plague had visited our shores only once or twice within living memory. The small-pox was always present, filling the churchyards with corpses, tormenting with constant fears all whom it had not yet stricken, leaving on those whose lives it spared the hideous traces of its power, turning the babe into a changeling at which the mother shuddered, and making the eyes and cheeks of the betrothed maiden objects of horror to the lover." De la Condamine, too, tells us that, among those who outlive an attack, many either totally or partly lose their sight or hearing, many are left consumptive, weakly, sick or maimed, many are disfigured for life by hideous scars, and become shocking objects to those who approach them. At a later period a Report of the Hospital for the Indigent Blind, quoted by Sir Gilbert Blane, informs us that two-thirds of those who applied there for relief had lost their sight by small-pox. Sir William Aitken affirms that 90 per cent of all cases of blindness met with in the bazaars in India are due to the same disease; and even the incomplete French statistics for the year 1871 record 24,004 cases of disfiguration and permanent injury caused by small-pox, over and above the 58,236 deaths attributable to that disease. No wonder the old-time proverb says, "From small-pox and love few remain free"!

From the foregoing some notion may be obtained of the state of affairs which existed when, towards the middle of the eighteenth century, the practice of inoculation was introduced into this country from the East, and prevailed until the discovery of vaccination by Jenner towards the close of the century.

The Relation of Cow-pox to Small-pox.—There is very little doubt in my own mind that human small-pox and cow-pox are derived from one and the same infection, though there are differences in their effects. Jenner firmly believed small-pox and cow-pox to be identical in their origin, and the most recent scientific investigations of the subject strengthen this view. These investigations are fully set forth by Dr. Copeman in an earlier section of this article.

It is alleged that Jenner's first hope, that vaccination would be an antidote "capable of extirpating from the earth a disease which is every hour devouring its victims—a disease that has ever been considered the severest scourge of the human race," has not been fulfilled. But this was not quite Jenner's more matured view; he was well aware of the fact that even an attack of natural small-pox does not invariably confer immunity from the disease; and, within a very few years of the discovery of vaccination, cases occurred in subjects who had been submitted to this operation. What Jenner really claimed was, to use his own words, that vaccination "duly and efficiently performed will protect the constitution from subsequent attacks of small-pox as much as that disease itself will. I never expected it would do more," he said, "and it will not, I believe, do less."

A century of experience has fully confirmed the accuracy of **Jenner's prognostication.** Vaccination "duly and efficiently performed" in infancy, and repeated at the age of puberty, has shown itself to be almost an absolute protection against small-pox; although in some few individuals the natural predisposition to the disease is so great that the artificial immunity dies out in a very few years. But it should be borne in mind that in those cases in which small-pox occurs after vaccination, the disease is, almost without exception, so far modified that its identity in its earliest stages is frequently unrecognised. To take a very recent illustration: in Blackburn the Medical Officer of Health met with a number of cases of small-pox in vaccinated persons, where the disease was so modified that the patients went about their work without being aware of the nature of the illness which was upon them.

With regard to the indisputable fact, clearly shown by the Registrar-General's returns from year to year, that **the mortality from small-pox has greatly decreased** within the present century, and especially within the last fifty years, the following table of the London death-rate from small-pox, given by Dr. Farr in his *Vital Statistics*, is most instructive:—

Years.	Average Annual Deaths per Million from all Causes.	Average Annual Deaths per Million from Small-pox.
1660–79	80,000	4170
1728–57	52,000	4260
1771–80	50,000	5020
1801–10	29,200	2040
1831–35	32,000	830

Continuing these figures for subsequent periods we get:—

Years.	Average Annual Deaths per Million from all Causes.	Average Annual Deaths per Million from Small-pox.
1838-53	24,900	513
1854-71	24,200	388
1872-82	22,100	262
1883-92	19,800	73

Unfortunately, complete statistics as to last century's small-pox for the whole country are not available, but, so far as they go, their testimony is the same. Since 1838, when registration became compulsory, we have definite information, and it will be seen that the decline has been very marked. Beginning with 1838 we find that the annual small-pox death-rates for the country for subsequent years are in consecutive order as follows:—1064, 589, 661, 400, 168 (*here occurs an interval of four years,* 1843 *to* 1846, *for which the figures are not available*), 246, 397, 264, 262, 389, 401, 171, 151, 131, 116, 202, 329, 193, 136, 64, 78, 286, 364, 301, 139, 114, 91, 67, 113, 1012, 821, 98, 88, 35, 99, 173, 74, 21, 25, 119, 50, 36, 82, 103, 11, 19, 37, 1, 0, 2, 15, 49, 27.

Changed Incidence of Small-pox since Vaccination.—But the most remarkable fact disclosed by careful examination of the small-pox statistics is the changed incidence of the disease in different age periods since the introduction of vaccination. Whereas in prevaccination times small-pox was essentially a disease of childhood—some 800 out of every 1000 small-pox deaths being those of children under five years of age, and 150 of the remaining 200 being of children between the ages of five and ten years (even as late as 1839, 88 per cent of the small-pox deaths in England were in children under ten years of age)—it has in recent years lost that peculiarity, as will readily be seen from the following table. In reading this table, it must be borne in mind that, although vaccination came into use early in the present century, no public provision for its gratuitous performance was made until 1840; it was not obligatory till 1853, and legislative arrangements for its systematic enforcement were not made until 1871.

TABLE.—Mean Annual Deaths from Small-pox at successive Life Periods per million living at each such Life Period—1847-53, 1854-71, and 1872-91.

Period.	All Ages.	0-5.	5-10.	10-15.	15-25.	25-45.	45 and upwards.
1. Vaccination optional, 1847-53	305	1617	337	94	109	66	22
2. Vaccination obligatory, but not efficiently enforced, 1854-71	223	817	243	88	163	131	52
3. Vaccination obligatory, but more efficiently enforced by vaccination officers, 1872-91	89	177	95	54	97	86	38

As pointed out by the Registrar-General in his 43rd Annual Report, with reference to a similar table, "The figures show conclusively that coincidently with the gradual extension of the practice of vaccination, there has been, in the first place, a gradual and notable decline in the mortality from small-pox at all ages; in the second place, that this decline has been exclusively among persons under ten years of age, and most of all among children under five; thirdly, that after the age of ten years the mortality, so far from having declined, has actually increased—very slightly among persons from ten to fifteen years of age, but very greatly for persons older than this; and, lastly, that the increase has been the greater the more advanced the time of life."

Recent Epidemics.—But it is by carefully analysing the facts relating to all the more important recent outbreaks of small-pox in this country that the value of efficient vaccination can best be established; for the statistical details of these epidemics, as given in the following table, are within our reach for purposes of verification; and, moreover, we have in them a safe and sure means of checking and exposing those methods of manipulation and distortion by which anti-vaccinators have attempted to discredit the older returns. Before studying the subjoined table it may not be out of place to ponder over the following utterances of M. de Freycinet when Minister of War in 1890: "One now sees, not only in France, but in Algeria, in Tunis, and in Tonquin, the army protected by the strict application of compulsory vaccination. . . . I cannot forget that, in 1870-1871, the German army, counting a million vaccinated and revaccinated men, only lost 459 men from small-pox in the two years, whereas our army, far less numerous, had, from the same cause, a loss of 23,400 men whom the prescient application of revaccination might have saved for the service of France."

TABLE SHOWING THE DISTRIBUTION OF SMALL-POX CASES AND DEATHS IN A NUMBER OF LARGE TOWNS BETWEEN THE YEARS 1887 AND 1896.

Period of Epidemic.	Towns.	Population.	Total Small-pox.			Under 10 Years of Age.									Over 10 Years of Age.								
						Vaccinated.			Unvaccinated.			Doubtful.			Vaccinated.			Unvaccinated.			Doubtful.		
			Cases.	Deaths.	Mortality per cent of Cases.	Cases.	Deaths.	Mortality per cent of Cases.	Cases.	Deaths.	Mortality per cent of Cases.	Cases.	Deaths.	Mortality per cent of Cases.	Cases.	Deaths.	Mortality per cent of Cases.	Cases.	Deaths.	Mortality per cent of Cases.	Cases.	Deaths.	Mortality per cent of Cases.
March 1887 to Feb. 1888	Sheffield	274,112	4,677	474	10·1	353	6	1·7	228	100	43·9	..	..	..	3774	194	5·10	322	174	54·2	..	..	..
Year 1892	,, ...	329,585	47	8	6·4	1	0	..	2	0	..	..	..	..	36	2	5·50	8	1	12·5	..	..	..
,, 1893	,, ...	333,922	102	4	3·9	6	0	..	7	0	..	..	..	..	79	3	8·70	3	0	..	7	1	14·2
Aug. 1892 to Dec. 1893	Leicester	184,547	357	21	5·8	2	0	..	107	15	14·0	..	..	..	197	2	1·0	51	4	7·8	..	..	..
May 1892 to March 1893	Warrington .	54,000	598	60	10·03	24	0	..	32	13	40·6	1	1	..	506	32	6·30	34	13	38·2	1	1	..
1891-2	Dewsbury ..	29,847	1012	110	10·8	45	1	2·2	174	56	32·1	..	..	..	601	17	2·8	192	86	18·7	..	..	..
1895-6	Gloucester ..	39,144	1979	434	21·9	26	1	3·8	680	279	41·0	..	..	..	1185	119	10·0	88	85	39·7	..	..	..
1892-3	Halifax	84,000	513	44	8·5	4	0	..	67	22	32·1	..	..	..	421	8	1·90	21	14	66·0	..	..	..
Jan. 1892 to June 1893	Oldham (Westhulme Hospital)	166,000	605	63	10·4	15	0	..	97	27	27·8	2	1	50·0	431	19	4·40	51	14	27·4	9	2	22·2
1893	Blackburn ..	124,000	79	8	10·1	3	0	..	..	..	..	1	1	..	68	2	2·90	4	3	75·0	3	2	66·6
1893	Bolton	117,000	44	6	13·6	1	1	..	.	..	..	..	.	..	30	0	..	6	3	50·0	7	2	25·0
1892	Bradford	219,262	25	4	16·0	2	0	..	1	1	..	..	..	..	20	2	10·00	2	1	50·0	..	..	..
1892	Brighouse ..	10,500	134	15	11·2	6	0	..	19	7	36·8	..	..	..	104	6	5·70	5	2	40·0	..	..	..
1893	,,		23	2	8·7	3	0	..	2	0	..	..	..	..	17	2	11·70	..	..	..	1	0	.
1893	Derby .. .	87,000	46	7	15·2	1	0	..	6	3	50·0	..	..	..	31	2	6·40	8	2	25·0	..	..	..
1892-3	Glasgow	677,883	250	18	6·9	10	0	..	2	2	100·0	..	..	..	238	11	4·60	9	5	55·5	..	..	..
1894	Hastings	63,466	86	9	10·4	4	0	..	10	4	40·0	..	..	..	63	3	4·70	2	0	..	7	2	28·5
1893	Huddersfield ..	97,500	48	2	4·1	..	..	..	1	1	..	..	..	..	35	0	..	11	1	9·1	1	0	..
1893	Keighley	32,000	72	7	9·7	1	0	..	24	4	16·6	..	..	..	30	1	3·30	17	2	11·7	..	..	..
1892	Liverpool	517,514	194	15	7·7	7	1	14·4	11	5	45·5	..	..	..	163	5	3·07	13	4	30·7	..	..	..
1892-3	Manchester ..	515,598	878	22	5·8	4	0	..	19	3	15·7	..	..	..	332	14	4·20	23	5	21·7	..	..	..
Nov. 1892 to June 1893	Middleton ..	22,162	22	2	9·1	2	0	..	3	1	33·3	1	0	..	11	0	..	2	1	50·0	3	0	..
April to July 1894	,,		34	4	11·7	0	0	..	8	2	25·0	..	..	..	25	1	4·00	1	1	..	..	..	..
1892	Ossett ..	11,100	19	1	5·2	0	0	..	1	1	..	..	..	..	18	0	..	..	..	..	..	..	..
1893	,,		26	0	0·0	0	0	..	1	0	..	..	..	..	23	0	..	2	0	..	..	..	..
1893	Pudsey	13,400	17	1	5·9	0	0	..	1	0	..	..	..	..	13	0	..	3	1	33·3	..	..	..
1893	Salford	203,431	174	21	12·0	7	0	..	20	7	35·0	..	..	..	125	8	6·40	17	5	29·4	5	1	20·0
1893	Southampton ..	65,325	152	8	5·2	13	0	..	8	3	37·5	1	0	..	103	0	..	7	4	57·1	20	1	5·0
1893	Swansea	93,816	23	1	4·3	3	0	..	..	..	..	..	..	..	19	0	..	1	1	..	..	..	..
Oct. 1892 to July 1893	York	66,912	72	7	9·7	2	0	..	5	1	20·0	..	..	..	56	4	7·10	8	1	12·5	1	1	..
						Under 15 Years of Age.									Over 15 Years of Age.								
1893	Birmingham[1] ..	487,897	970	70	7·1	107	0	..	69	20	29·0	4	0	..	740	88	5·10	36	12	33·3	23	0	..
1887-8	Bristol[1] ..	225,028	327	37	11·3	64	0	..	22	12	54·5	..	..	..	208	11	5·50	33	14	42·2	..	..	..
1893	,,		164	19	11·5	12	0	..	15	6	40·0	..	..	..	126	8	6·33	11	5	45·4	..	..	..
1893	Walsall[1]	74,000	778	71	9·1	123	2	1·6	141	41	29·0	4	3	75·0	431	4	0·90	66	20	30·3	13	1	7·7
	Totals		14,065	1570	11·14	851	12	1·4	1783	636	35·6	14	6	42·8	10,259	518	5·0	1057	384	36·3	101	14	18·8

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[1] In these instances the available statistics only enable the cases to be distributed according as they were under or over 15 years of age, instead of under or over 10 years of age.

Immunity of vaccinated children under 10 from death by small-pox.—It would, of course, occupy too much space to discuss in detail each individual epidemic enumerated in the above table; but the more important outbreaks will be dealt with separately, so as to establish beyond dispute that, in the epidemics referred to, the vaccinated children under ten have been almost immune from death by small-pox, and that when they have contracted the disease they have suffered from it in its mildest form. On the other hand, the unvaccinated children have suffered in every instance far more severely; some 20 to 50 per cent of the cases amongst them having terminated fatally. It must be borne in mind that in the enumerated towns and districts the vaccinated are frequently in the aggregate seven or eight times as numerous as the unvaccinated; that they include a large proportion of children whose vaccination has been very imperfectly performed, and that both categories are drawn from the same aggregate population living, broadly speaking, in the same sanitary conditions. The only broad line of distinction between the two classes of children is in regard to their vaccination; and this only can account for the wide difference which exists between the rates of attack and mortality from small-pox in the two classes.

Beginning with *the Sheffield epidemic of* 1887-88, we have to deal with a town which is not a centre of antivaccination. Indeed, the law had been carried out so well there that at the time of the outbreak some 97 or 98 per cent of the population were more or less efficiently protected by vaccination. That an epidemic of small-pox should occur in so "well-vaccinated" a town was a source of great jubilation to antivaccinators—for a time. Fortunately the vast importance of the occurrence was so evident, that an exhaustive investigation of the matter was wisely instituted at once by the Government through the Local Government Board. This arduous task was entrusted to Dr. F. W. Barry; and the facts disclosed in that gentleman's report form such a monumental testimony to the value of vaccination, that nowadays antivaccinators seldom refer to the Sheffield epidemic.

Dr. Barry began his inquiry at a time when some 300 fresh cases of small-pox were occurring each week in the borough; and he was consequently in a position, by prompt personal inquiry and personal observation, to place beyond cavil many matters of fact which otherwise might have been disputed and distorted. He proceeded with assistants to make a house-to-house census of the infected localities, which he found to contain 274,112 inhabitants, of whom 268,397 were classed as vaccinated and 5715 as unvaccinated. Under ten years of age there were 68,236 vaccinated children, and of these 353 (or ·51 per cent) were attacked, and 6 (or ·009 per cent) died; whilst at the same age there were only 2259 unvaccinated children, of whom 228 (or 10·09 per cent) were attacked, and 100 (or 4·4 per cent) died. For obvious reasons children under the age of one month were excluded. Above the age of ten there were 196,905 vaccinated persons, and of these 3774 (or 1·9 per cent) were attacked and 194 (or ·09 per cent) died; whilst there were only 3429 unvaccinated persons, and of these 322 (or 9·4 per cent) were attacked, and 174 (or 5·07per cent) died. There were in addition 3256 vaccinated and 27 unvaccinated persons whose ages could not be ascertained, and who have therefore been excluded from the above calculations, together with the 24 and 2 cases of small-pox which occurred among them respectively. In dealing with the Sheffield epidemic it is impossible to refrain from quoting the following paragraphs from the late Sir George Buchanan's masterly analysis of Dr. Barry's report:—"First, of the children under ten years of age living in Sheffield during 1887-88 under the common conditions of infection in the whole borough:

Per thousand of the number of children in each class—

The attack-rate of the vaccinated was	5	
The attack-rate of the unvaccinated was	101	
The death-rate of the vaccinated was		0·09
The death-rate of the unvaccinated was		44

"Under the general circumstances of the Sheffield epidemic, therefore, the vaccinated children had, as compared with the unvaccinated children living in the town, a twenty-fold immunity from attack by small-pox, and had a 480-fold security against death by small-pox. The above relates to the general child-population of the borough"; but "children living in houses actually invaded were, of course, exposed to an intenser and more continuous infection." "Next, concerning persons over ten years of age living in Sheffield during 1887-88 under the common conditions of infection of the borough. The vaccinated and unvaccinated members of this class are found to have always differed to a considerable degree from each other, both in regard of attack and of death, and also whether the borough as a whole or its component subdistricts be examined. But this degree of difference (considerable though it has been) has not been nearly so large as in the class of children.

Per thousand of the number of persons over ten in each class:—

The attack-rate in persons twice vaccinated was	3	
The attack-rate in persons once vaccinated was	19	
The attack-rate in persons not vaccinated was	94	
The death-rate among persons twice vaccinated was		0·08
The death-rate among persons once vaccinated was		1
The death-rate among persons not vaccinated was		51

"Under the general circumstances of the Sheffield epidemic, therefore, the twice vaccinated persons over ten years of age, as compared with the unvaccinated persons of the same age living in the town, had a thirty-one-fold immunity against attack by small-pox, and had a 640-fold security against death by small-pox." Surely the facts of the Sheffield epidemic, and the strictly logical and justifiable conclusions drawn therefrom, bear unanswerable testimony to the value of vaccination?

Now let us turn to *Leicester*, which is well known to have become the chief centre of the antivaccination movement. There vaccination has been practically suspended for several years past, and a gigantic experiment tried of endeavouring to cope with small-pox by, curiously enough, substituting for compulsory infantile vaccination another set of even harsher compulsory measures—compulsory isolation, compulsory "quarantine" for twelve or fourteen days, and such like.

As the comparative immunity from small-pox of "unvaccinated" Leicester has become a stock argument among antivaccinators, it is especially instructive to see how the town fares when the disease happens to obtain a footing in it. The Leicester epidemic of 1892-3 was investigated on behalf of the Royal Commission on Vaccination by Dr. Sidney Coupland, and his report gives the following facts:—

Of children under 10 years of age there were—
  Vaccinated cases, 2 ; deaths, 0 . . . . = 0·0 per cent.
  Unvaccinated cases, 107 ; deaths, 15 . . = 14·0 „
Of persons over 10 years of age there were :—
  Vaccinated (including doubtful) cases, 197 ; deaths, 2 = 1·0 per cent.
  Unvaccinated cases, 51 ; deaths, 4 . . . = 7·8 „

These figures are convincing enough by themselves, but they gain additional significance when the cases are arranged according to the severity of the small-pox. Dr. Coupland's report shows that—

Of the 199 vaccinated cases :—
  17 or 8·5 per cent were confluent.
  20 „ 10·1 „ „ coherent.
  50 „ 25·1 „ „ discrete.
  112 „ 56·3 „ „ mild.
Of the 158 unvaccinated cases :—
  79 or 50·0 per cent were confluent (including malignant).
  36 „ 22·8 „ „ coherent.
  28 „ 17·7 „ „ discrete.
  15 „ 9·5 „ „ mild.

Turning to the *Warrington* epidemic of 1892-3, we find from the report of Dr. T. D. Savill, who investigated the matter on behalf of the Royal Commission, that—

Of children under 10 attacked by small-pox—
  33 were vaccinated, and 2 (or 6 per cent) died.
  32 were unvaccinated, and 12 (or 37·5 per cent) died.
Of persons over 10 years attacked—
  560 were vaccinated, and 36 or (6·4 per cent) died.
  36 were unvaccinated, and 12 (or 33·3 per cent) died.

During the epidemic 457 houses were invaded, but as regards 20 of these houses Dr. Savill could not obtain precise information. Taking, however, the facts ascertained as to the remainder, Dr. Savill reports that in those 437 houses there resided 2535 persons, of whom 41 were stated to have had small-pox in previous years; five of these latter were again attacked in 1892-3: of the remaining 2494 persons, 688 were under and 1806 were over 10 years of age.

Of the children under 10 years 633 were vaccinated, of whom 28 (or 4·4 per cent) were attacked; and 55 were unvaccinated, of whom 30 (or 54·5 per cent) were attacked.

Of the 1806 persons over 10 years of age, 1754 were vaccinated, of whom 525 (or 29·9 per cent) were attacked; whilst 52 were unvaccinated, and of these 30 (or 57·6 per cent) were attacked.

With reference to the contrast here shown between the attack-rate in the case of the vaccinated and of the unvaccinated living in infected houses, Dr. Savill says: "I could ascertain no reason for this remarkable difference in the attack-rate in the two classes, unless the fact of vaccination protected the vaccinated persons from being attacked by small-pox. Being members of the same families, they lived in the same houses (which, be it noted, were remarkably uniform), ate the same food, often did the same work, and were exposed to the same hereditary and external influences."

As regards the character of the disease, Dr. Savill reports on 661 of the cases, of which 593 were vaccinated or doubtful, and 68 were unvaccinated.

Of the 593 vaccinated cases—

323 or 54·5 per cent were mild.
141 ,, 23·8 ,, ,, discrete.
129 ,, 21·8 ,, ,, confluent.

Of the 68 unvaccinated cases—

3 or 4·4 per cent were mild.
17 ,, 25·0 ,, ,, discrete.
48 ,, 70·6 ,, ,, confluent.

[Amongst the confluent cases here are included the malignant or hæmorrhagic.]

Taking again the 65 cases under 10 years of age.

Of the 33 vaccinated cases—

24 or 72·7 per cent were mild.
7 ,, 21·2 ,, ,, discrete.
2 ,, 6·1 ,, ,, confluent.

Of the 32 unvaccinated cases—

2 or 6·2 per cent were mild.
7 ,, 21·9 ,, ,, discrete.
23 ,, 71·9 ,, ,, confluent.

The Warrington outbreak, also, will illustrate the preventive power of revaccination; for Dr. Gornall, the local health officer, records that of 824 persons in the military barracks not one was attacked by the disease, and that no case occurred amongst the 117 revaccinated persons in the postal service, nor in the police force, whose members were all revaccinated.

Dewsbury is another centre of antivaccination, and the behaviour of the outbreak of small-pox there in 1891-92, which was investigated by Dr. Coupland on behalf of the Royal Commission, is instructive.

Of children under 10 years attacked there were—
    45 vaccinated (or doubtful), of whom 1 (or 2·2 per cent) died.
    174 unvaccinated, of whom 56 (or 32·1 per cent) died.
Of persons over 10 years attacked there were—
    601 vaccinated (or doubtful), of whom 17 (or 2·8 per cent) died.
    192 unvaccinated, of whom 36 (or 18·7 per cent) died.

Here also a comparison of the rates of attack of the vaccinated and unvaccinated, and of the severity of the disease in each class, gives the same marked results as in the case of all the other epidemics already examined.

Gloucester has afforded one of the most instructive object lessons of recent times in favour of vaccination. Formerly vaccination was fairly well carried out in Gloucester; but in 1886 an agitation in opposition to vaccination was organised, the local authorities soon ceased to enforce the law, and default so rapidly grew that between 1889 and 1895 upwards of 80 per cent of the children born were left unvaccinated. At last, however, the inevitable day of reckoning arrived, and during the early months of 1896 the ancient city was struggling almost hopelessly against a severe epidemic. The Royal Commission on Vaccination, then sitting, caused a careful investigation to be carried out by Dr. Sidney Coupland, and from his report it appears that—

Of the children in the city under 10 years there were attacked—
    26 vaccinated, of whom 1 (or 3·8 per cent) died.
    680 unvaccinated, of whom 279 (or 41 per cent) died.
Of persons over 10 years of age there were attacked—
    1185 vaccinated, of whom 119 (or 10 per cent) died.
    88 unvaccinated, of whom 35 (or 39·7 per cent) died.

Dr. Coupland was only able to obtain definite information with reference to 899 out of the 1097 houses invaded by the disease. In these 899 houses there resided 4861 persons. Of these 3386 had been vaccinated, or were said to have been vaccinated, at some time in their lives prior to the epidemic; the remaining 1475 were unvaccinated at the time their houses became infected; though a considerable proportion of them were subsequently scared by the epidemic into seeking vaccination.

Of the children under 10 there were—
    272 vaccinated, of whom 24 (or 8·8 per cent) were attacked.
    1331 unvaccinated, of whom 617 (or 46·3 per cent) were attacked.
Of the persons over 10 there were—
    3114 vaccinated, of whom 1004 (or 32·2 per cent) were attacked.
    144 unvaccinated, of whom 72 (or 50 per cent) were attacked.

It is not possible to estimate fully the total financial loss sustained by the citizens of Gloucester during this disastrous epidemic, and in consequence of it; but, apart altogether from the cost of the 20,000 vaccinations and revaccinations which were performed during the epidemic, the expenses of the Town Council, as the sanitary authority, solely in their struggle with the epidemic, amounted to upwards of £15,000. This alone is a formidable price to have to pay for an unwise experiment.

The foregoing facts respecting the recent epidemics in Sheffield, Leicester, Warrington, Dewsbury, and Gloucester, have been taken from the elaborate Report of the Royal Commission on Vaccination, from which are also taken the two following very instructive tables summarising some of the more striking features:—

TABLE showing the Rate of Attack by Small-pox among the Vaccinated and the Unvaccinated, under and over 10 years of age respectively.

	Attack Rate under 10 Years.		Attack Rate over 10 Years.	
	Vaccinated.	Unvaccinated.	Vaccinated.	Unvaccinated.
Sheffield . . .	7·9	67·6	28·3	53·6
Leicester . . .	2·5	35·3	22·2	47·6
Warrington . .	4·4	54·5	29·9	57·6
Dewsbury . . .	10·2	50·8	27·7	53·4
Gloucester . . .	8·8	46·3	32·2	50·0

TABLE showing (by percentages) what proportions of the Cases amongst the Vaccinated and Unvaccinated respectively were attacked by the milder and by the severer types of Small-pox.

		Milder Types (Varioloid or Mild and Discrete).	Severer Types (Coherent and Confluent).
Sheffield	Vaccinated . .	82·8	17·2
	Unvaccinated . .	18·5	81·5
Leicester	Vaccinated . .	81·4	18·6
	Unvaccinated . .	27·2	72·8
Warrington	Vaccinated . .	78·2	21·8
	Unvaccinated . .	29·4	70·6
Dewsbury	Vaccinated . .	82·0	18·0
	Unvaccinated . .	23·1	76·9

These tables require no explanation; they speak eloquently, and show in an unmistakable fashion the beneficial influence of vaccination.

Some of the features of other outbreaks of small-pox deserve also some notice here. In *Halifax* the antivaccinators have, during the last seven or eight years, gained such an ascendency on the Board of Guardians that the Vaccination Acts have become almost a dead letter in the town. This is shown by the fact that in 1891 only 516out of 4868 children born were vaccinated. Halifax was visited by small-pox in 1892 and 1893, and during the course of eighteen months 513 cases were admitted into the Fever Hospital, and 44 (or 8·5 per cent) died. Of these 425 were vaccinated, and of them only 8 (or 1·8 per cent) died. The remaining 88 were unvaccinated, and of them 36 (or 40·9 per cent) died. Looking more closely at the figures, we find that there were no vaccinated cases whatever under five years of age; but that 50 unvaccinated children of that age-period were attacked, and of them 20 (or 40 per cent) died. Between five and ten years of age there were 4 vaccinated cases, all mild and non-fatal; whilst there were 17 unvaccinated cases of that age, 9 of them confluent and 2 fatal. Above ten years of age there were 421 vaccinated cases, 325 of them being "discrete" or mild, 96 of them "semi-confluent" or "confluent," or severe, and only 8 (or 1·8 per cent) of them fatal; whilst of the 21 unvaccinated cases all were severe, and 14 (or 66 per cent) were fatal. Two revaccinated persons were attacked, but in one of them the revaccination had taken place thirty-four years previously, and in the other the operation had been inefficiently performed five years previously.

The vaccination of children in *Oldham* is about on a par with that which obtains in Halifax. It will be seen from the table that, between January 1892 and June 1893, 605 cases of small-pox were treated in the Westhulme Hospital. Of these 15 were vaccinated children under 10 years of age, and all recovered; 97 were unvaccinated children under 10, and 27 (or 27·8 per cent) died; 431 were vaccinated adults, and of these 19 (or 4·4 per cent) died; whilst 51 were unvaccinated adults, of whom 14 (or 27·4 per cent) died.

It passes the wit of man to understand how, in the face of such experiences as these, towns like Halifax and Oldham are still led astray by the sophistries of the local opponents of vaccination.

Besides showing the usual results noted in other epidemics, the *Blackburn* visitation in 1893 demonstrated very clearly the protection afforded by revaccination after exposure to infection. Of 243 persons detained in quarantine for 14 days, 211 were revaccinated, 15 were already sufficiently protected by revaccination or a previous attack, and 17 were not revaccinated. Of the revaccinated 211, 2 caught the disease; 1 having been exposed to the infection four days and the other five days before the performance of the operation. Of the 17 persons who were not revaccinated 5 caught the disease. These facts surely go to show that, if vaccination and revaccination were efficiently and judiciously carried out, the great expense and restriction of individual liberty involved in these "quarantines" could be avoided. It is interesting to note that Dr. Wheatley, the Medical Officer of Health, found that a large number of the inmates of common lodging-houses had been revaccinated; some in the army or navy, others in public institutions. There can be no doubt that but for this large amount of revaccination small-pox would have spread to a much greater extent in the lodging-houses than it did.

Although the total number of cases of small pox in *Huddersfield* in 1893 was small, the epidemic teaches the same lessons as the more serious outbreaks. Forty-six of the 48 cases were amongst persons over twenty years of age, and the remaining 2 were under twelve, 1 being an unvaccinated child of five, daughter of an antivaccinator, who very wisely had the rest of his family vaccinated; the other was a boy of twelve practically unvaccinated, because, although subjected to the operation in infancy, "it did not take." Twelve of the patients were unvaccinated, and the only 2 deaths occurred amongst them. Writing of these fatal cases, Dr. Kaye, Medical Officer of Health, remarks, "If any convincible antivaccinator could have witnessed the horrible condition of both these fatal cases—features swollen beyond recognition, and covered from head to foot with loathsome-smelling scabs, and totally incapable of doing anything for themselves—I do think he would have seriously reconsidered his position."

As *Keighley* is a hot-bed of antivaccinism, the small-pox epidemic which occurred there in 1893 is worth looking into. Of the 72 cases of the disease, 31 were vaccinated and 41 unvaccinated; but only 1 of the former died, whilst 6 of the latter were fatal. Only 1 vaccinated child under ten years of age was attacked, the disease being of a mild form; whilst 24 unvaccinated children were attacked, 17 of whom had the disease in a confluent form, and 4 of whom died. There were altogether 40 "confluent" or "semi-confluent" cases, of which 33 were unvaccinated, and only 7 vaccinated; 4 of the latter being "semi-confluent."

The epidemics in *Birmingham*, *Salford*, *Southampton*, and *Swansea* tell a similar tale.

As an illustration of the certainty with which small-pox singles out the unvaccinated for attack, Dr. Gale, Medical Officer of Health for the Ecclesall Bierlow Rural Sanitary District, records the following interesting particulars of an outbreak in a family at Green Oak in 1893:—

Father, vaccinated in infancy, not attacked.
Mother, vaccinated and revaccinated, not attacked.
S., aged 17 years, unvaccinated, severe small-pox, recovered.
W., „ 13 „ " " "
A., „ 11 „ unvaccinated, severe small-pox, died.
E., „ 10 „ " " "
J., „ 8 „ vaccinated and revaccinated, not attacked.
C., „ 6 „ vaccinated six days before the first symptoms of the disease, too late to give protection, severe small-pox, recovered.
N., aged 4 years, vaccinated, not attacked.
G., „ 2 „ " "

That *vaccination affords protection even after exposure to the disease* has already been pointed out in dealing with the Blackburn epidemic (p. 670); but a few further examples illustrating this rule may not be out of place. Thus Dr. Niven, in his report on the Oldham outbreak, emphasises the fact that vaccination or revaccination immediately after exposure to the infection (especially within three days after the appearance of the eruption in the patient first attacked) reduces, practically to a minimum, the risk of subsequent development of the disease in the individuals who have been exposed. Again, during the Southampton outbreak of 1893, two constables had occasion to visit a house in which a boy was suffering from small-pox; the nature of the illness was not discovered till after their visit. Dr. Harris, the Medical Officer of Health, immediately offered to vaccinate both the officers, but only one would accept the proposal, with the result that he escaped; while the other, who refused, was admitted to the hospital a fortnight later suffering with severe "confluent" small-pox, from which he nearly lost his life. Dr. Gale, too, reports that during an epidemic at Totley Rise an unvaccinated child was attacked by small-pox. The mother immediately brought her three other children to the vaccination station, where they were successfully vaccinated; and although they continued to reside with their ailing sister not one of them was attacked. Finally, Dr. Cunningham, the Health Officer for Oldbury, mentions that of all those persons who sought revaccination during the small-pox prevalence in 1893, not one contracted the disease; although some of them are known to have been in actual contact with infection.

The influence of vaccination in mitigating the severity of an attack of small-pox has perhaps been sufficiently proved by the foregoing statistics of actual epidemics. But it is also well shown in the official records of "pitting" or permanent disfigurement following the disease, and again by the length of stay of patients in hospital. From Dr. Barry's report on the Sheffield epidemic of 1887-88, we find that out of 451 vaccinated children under ten years of age attacked by small-pox, only 24 showed any "pitting" on recovery; whilst "in nearly all the children of the unvaccinated class, who were incidentally inspected in the course of the inquiry, the attack of small-pox was of a severe type, and in the majority of cases was followed by considerable pitting." Dr. Priestley, again, in his full and precise report of the Leicester outbreak, states that of 134 unvaccinated cases of small-pox which recovered as many as 112 were more or less "pitted," most of them severely; whilst out of 177 vaccinated individuals who recovered only 43 had any "pitting" whatever, and in 4 cases only was the "pitting" at all severe.

As regards the duration of the disease in vaccinated patients the experience of Leicester during the outbreak of 1892-3 was that amongst children under ten years of age the stay in hospital of the vaccinated was 14·5 days, and of the unvaccinated 43·7 days. Amongst persons over ten years of age the average stay was 28·6 days in the vaccinated, 14 days in those who had previously had small-pox, but as much as 44·2 days amongst the unvaccinated. In the City Small-pox Hospital of Birmingham during the first eleven months of 1893 the following instructive facts were observed:—

	Average No. of Days in Hospital.
All vaccinated cases	30
Cases with 1 mark	34
,, 2 marks	33½
,, 3 ,,	29¼
,, 4 ,,	28
,, 5 ,,	26½
Unvaccinated cases	50

In Keighley the average duration of the illness was 36 days among the vaccinated, as compared with 53 days in the unvaccinated. This is, broadly speaking, the experience of most epidemics; though Mr. E. C. Greenwood, the Public Vaccinator of St. Marylebone, states that, in an epidemic in that parish, the average stay of the unvaccinated was 35 days; whilst that of the vaccinated was 25 days.

Immunity of doctors, nurses, and others in small-pox hospitals.—We now come to the consideration of one of the most powerful arguments in favour of the usefulness of efficient vaccination and revaccination; to wit, the comparative immunity of the vaccinated and revaccinated doctors, nurses, and others employed generally in and around small-pox hospitals. Writing on this subject in Quain's *Dictionary of Medicine*, Dr. Collie, who for many years was superintendent of one of the hospitals of the Metropolitan Asylums Board, says:—"During the epidemic of 1871, 110 persons were engaged in the Homerton Fever Hospital in attendance upon the small-pox sick; all these, with two exceptions, were revaccinated, and all but these exceptions escaped small-pox. The experience of the epidemic of 1876-77 was of the same kind, all revaccinated attendants having escaped, whilst the only one who had not been vaccinated took the disease and died of it. So, in the epidemic of 1881, of 90 nurses and other attendants of the Atlas Hospital Ship (small-pox), the only person who contracted small-pox was a housemaid who had not been revaccinated." In 1885 a Vaccination Committee of the Epidemiological Society of London independently investigated this subject, confining its attention to those "in personal attendance on cases of small-pox"; with the result that out of 1500 such attendants only 43 were found to have contracted small-pox, "and not one of these 43 had been revaccinated" (see *Transactions of the Epidemiological Society*, vol. v. New Series). Further, on turning to the Reports of the Metropolitan Asylums Board for 1892, we find a summary by Dr. T. F. Ricketts, the medical superintendent of the Small-pox Hospital Ships on the Thames, showing that out of 1201 persons who had been engaged on board the ships since 1884, and who had therefore been exposed to the infection of small-pox, only six contracted the disease, and all recovered. One of these cases was a stoker who had become infected before joining the staff; two of the others were vaccinated unsuccessfully on the day of joining only; another was vaccinated unsuccessfully on the day after joining the staff, and with partial success a week later, with the result that the attack consisted of "a few spots" only; another of the patients was vaccinated, after joining, on three occasions unsuccessfully;

and the sixth case was in a ward-maid who was vaccinated, after joining, on three occasions unsuccessfully; on the fourth trial successfully, but too late to prevent her being attacked by small-pox: though no doubt it was owing to the vaccination that her attack was one of "very mild discrete" small-pox. In Dr. Ricketts' report for 1893 we find that of the 307 persons employed on the hospital ships during the year six contracted small-pox and all recovered. In one of these patients the disease appeared three days after joining the ship, showing that the infection had been contracted from an independent source. Of the other five cases vaccination in two instances was altogether unsuccessful; and in three it was not successful until the third attempt: meanwhile the small-pox had laid hold of these imperfectly protected individuals, though the attacks were not severe or fatal in any case. During 1893, also, five workmen temporarily employed at the ships caught small-pox and recovered. Four of these men had foolishly evaded vaccination; whilst the fifth, whose attack was a mild one, had been vaccinated twice unsuccessfully. The failure to secure prompt success in the vaccination of some of these persons is accounted for by Dr. Ricketts by the fact that stored lymph has necessarily to be used at the ships.

Again, throughout the country the experience as to the immunity of properly revaccinated small-pox nurses and attendants is similar to that of London. At Leicester, where the authorities, who laugh vaccination to scorn, have been challenged in vain to complete their gigantic experiment by employing none but unvaccinated people as nurses and attendants at their small-pox hospitals, the influence of vaccination and revaccination in protecting the nurses from small-pox has been characteristically illustrated. During the epidemic of 1892-93 there were forty officials connected with the Leicester Small-pox Hospital. Of these, 34 were efficiently protected, either by previous small-pox or by revaccination; and they all escaped the disease with one exception, that of a nurse who had been revaccinated ten years previously and whose attack was a mild one. The remaining six, however, were inefficiently protected; they refused to be revaccinated, and five of them were attacked by small-pox. The only inefficiently protected official who escaped was the matron, who, of course, was not much exposed to the contagion. At Warrington, in the epidemic of 1892-93, no case occurred amongst the 23 nurses and others who were exposed to contact with small-pox in the discharge of their duties at the local small-pox hospital; but two cases of the disease occurred in the only two members of the staff who were not revaccinated at the beginning of the outbreak. In Halifax only one of the hospital officials was attacked in 1892-93, and that during the first week of the epidemic and before revaccination; all the others were revaccinated, and all escaped. During the 1893 epidemic in Derby the whole of the staff connected with the hospital had been revaccinated, and not one of them was attacked with the disease. As regards the hospital at Salford, during the epidemic of 1893, Mr. Mullen, the medical superintendent, reports that "with very few exceptions all the nursing staff of the Ladywell Sanatorium, all of whom have been successfully revaccinated, were afforded the opportunity of adding to their experience by being detailed in turn for attendance on small-pox patients. Not one of the staff contracted the disease." At the Southampton Fever Hospital all persons employed during the small-pox epidemic of 1893 were revaccinated before beginning duty; and in spite of their daily close contact with the disease, in no instance did a member of the staff contract small-pox. Dr. Hill of Birmingham reports that during the epidemic there in 1893 over 100 persons were engaged on the staff of the City Small-pox Hospital, all of whom had been recently revaccinated; not one of them contracted small-pox. The same is the experience at the hospitals at the numerous other places of which information is available; and Dr. G. R. Macgregor, in his annual report for the Bingley Local Board District, declares that "to such an extent has successful revaccination impressed itself upon me, that I have no fear myself personally of the closest possible contact with the most malignant cases of small-pox, and I have no fear whatever in advising persons so successfully revaccinated to have the most intimate contact with even the most virulent cases of small-pox."

Now how do the above observations compare with those of attendants on other infectious fevers? Taking the year 1893, we find that of 2484 persons employed in the nine metropolitan fever hospitals, 130 became infected, and 2 died: 4 assistant medical officers, 10 nurses, 43 assistant nurses, and 16 ward servants were attacked by scarlet fever; 2 assistant medical officers, 6 nurses, and 15 assistant nurses by diphtheria; 2 nurses and 3 assistant nurses by enterica, and so forth. Again, how comes it that the deaths of medical men from small-pox are but 13 per million as against 73 per million of the general population; whereas, in scarlet fever, against which doctors have no special protection, there is the remarkable fact that 59 medical men per million die from this cause, as against 16 per million of the public?

Typhus fever, also, is a disease which numbers amongst its victims a large proportion of the medical men who are brought within its reach in pursuance of their vocation. At the London Fever Hospital during the period 1862-70, when large numbers of typhus patients were treated, the average number of attendants of all kinds employed in the course of a single year was about 100; and the average annual number of cases of typhus occurring amongst that staff was 19·2. Between 1862 and 1866 three resident medical officers and six other medical assistants caught typhus, and one died from the disease.

When these indisputable facts are borne in mind, and accentuated by the remarkable immunity enjoyed in the presence of small-pox by the revaccinated postmen, policemen, soldiers, sailors, and others, the propriety not only of compulsory primary vaccination, but of compulsory revaccination at puberty, is irresistibly forced upon us.

Necessity of efficient vaccination.—It has already been shown that in the variety of lessons taught by a careful study of recent statistics, and a comparison of them with the older figures, the most obvious and important is—allowing, of course, for a few exceptions which prove the rule — that efficient vaccination in infancy affords an almost absolute immunity from small-pox up to about ten years of age, and that after that date the operation must be efficiently repeated. Efficiency, however, is essential. Certain antivaccinators assume that all vaccination—good, bad, and indifferent—must be regarded as equally protective, or rather unprotective, against small-pox. It would be scarcely less absurd to argue that the mere visit to a public vaccinator's surgery should be regarded as proper vaccination. Vaccination may and does vary very much in quality; and the more closely the vaccination of the patients in recent epidemics has been studied, the more obvious has it become that a deplorably large proportion of the nominally vaccinated to-day have been most inefficiently vaccinated, and are consequently in many cases almost unprotected against an attack of small-pox. Nothing has done so much to injure the cause of vaccination as the fact that, in consequence of inefficient vaccination, cases of post-vaccinal small-pox, modified though they be by the vaccination, occur in every epidemic. So long as medical men, in their mistaken good nature, are found ready to yield to the ignorance or vanity of applicants for vaccination, and to make only one or perhaps two insignificant insertions of lymph in a child's arm, and to certify cases of that kind as successfully vaccinated, so long shall we have to struggle against the fallacies and sophistries of antivaccinators. Better by far let such applicants depart with their children unvaccinated than place them in a state of false security, and at the same time endanger the practice of one of the greatest prophylactics of modern times.

How, then, is efficient vaccination to be secured?—To attain this end the official instructions of the Local Government Board prescribe that public vaccinators shall "in all ordinary cases of primary vaccination, make such insertions of lymph as will produce at least four separate good-sized vesicles, or groups of vesicles, not less than half an inch from one another. The total area of vesiculation on the same day in the week following the vaccination should not be less than half a square inch."

There is abundant evidence, both from earlier and recent epidemics, of the correctness of this instruction, and of the need for its observance as a minimum of efficiency. Between 1836 and 1867 the late Mr. Marson—who, as surgeon of the London Small-pox Hospital, had exceptional opportunities of making trustworthy observations over an extended period—recorded the facts concerning 13,755 cases of small-pox. The results are shown in the following table, which was laid by Dr. Thorne Thorne before the Royal Commission on Vaccination:—

13,755 Cases of Small-pox classified, according to the Vaccination Marks borne by each Patient respectively.	Percentage of Death in each Class respectively.	
	1836–1851 (3094 cases).	1852–1867 (10,661 cases).
Stated to have been vaccinated, but having no cicatrix	21·7	39·4
Having 1 vaccine cicatrix	7·6	13·8
,, 2 ,, cicatrices	4·3	7·7
,, 3 ,, ,,	1·8	3·0
,, 4 ,, ,,	0·7	0·9
Unvaccinated	35·5	34·9

Dr. Thorne Thorne also called the attention of the Commissioners to a summary by Dr. Seaton of Mr. Marson's observations :—"Summarily, the 32 years' observations show that, of 13,755 reputedly vaccinated patients admitted into the hospital during that period, the vaccination was very defective in 11,172, of whom 1027 died; was reasonably good (as represented by three characteristic marks) in 1079, of whom 21 died; and was quite up to the now acknowledged standard in 1505, of whom only 13 died." Dr. Seaton also pointed out that, in the Stockwell and Homerton Hospitals, "of 2382 patients having marks of vaccination, 1866 had characteristic marks (one or more), and 516 had marks which were bad or indifferent. Of the former 70 died, or 3·9 per cent; of the latter 129, or 25 per cent." Again, in the following table we have a summary as regards 10,403 small-pox patients who came under the observation of Dr. W. Gayton, whilst he was Medical Superintendent of the Homerton Small-pox Hospital, and of the North-Western Fever Hospital of the Metropolitan Asylums Board :—

Condition as to Vaccination.	Under 10 Years.			Over 10 Years.		
	Cases.	Deaths.	Percentage.	Cases.	Deaths.	Percentage.
Vaccinated with good marks	267	2	·75	1818	60	3·3
Vaccinated with imperfect marks	714	48	6·72	4140	407	9·8
Said to have been vaccinated, but no visible marks	325	87	26·7	970	265	27·3
Not vaccinated	1187	563	47·4	982	375	38·2

Dr. Gayton, in his evidence before the Royal Commission, discussed these 10,403 cases minutely; and pointed out, amongst other noteworthy facts, that "the imperfectly vaccinated, the doubtfully vaccinated, and those confessedly unvaccinated, give a general though not an absolute support to the doctrine that the law of natural small-pox is that its fatality is greatest in infancy, decreases to a minimum about the third quinquennium of life, and then rises again. . . . The regular rise in mortality with increasing age exhibited by the well vaccinated is quite in accord with the teaching and opinion of those who insist upon the necessity of revaccination. . . . Of the 10,403 patients, 61 only consisted of well-vaccinated children under five years of age, with no deaths; 182 were imperfectly vaccinated, with 21 deaths; 118 were doubtfully vaccinated, with 47 deaths; while 677 were confessedly not vaccinated, and among them there were 383 deaths. Of those under two years of age, 4 were well vaccinated, and there were no deaths; 32 were imperfectly vaccinated, with 3 deaths; 22 were doubtfully vaccinated, with 9 deaths; and 276 were unvaccinated, with 181 deaths."

Special attention was given to this question of "marks" by the medical men who investigated the recent outbreaks of small-pox for the Royal Commission, with the result that the vaccination marks in 6839 cases were ascertained. These cases are classified as follows:—

1 mark,	1357 cases, with	85 deaths,	or 6·2 per cent.
2 marks,	1971 „ „	115 „	„ 5·8 „
3 „	1997 „ „	75 „	„ 3·7 „
4 „	1514 „ „	34 „	„ 2·2 „

During the year 1893 there were 46 cases of small-pox in Derby. Of these, 14 showed no marks of vaccination; 5 showed only 1 mark each (good in 4 instances); 11 showed 2 marks each (good in only 4 cases); 8 had 3 marks each (good in 6 cases), and 7 had 4 marks each (good in 5 cases): so that only 11 of the persons who suffered from small-pox were properly vaccinated. Of the 14 patients showing no marks of vaccination, 5 (or 35·7 per cent) died; of the remaining 32 patients who had been vaccinated, only 2 died (or 6·2 per cent), and both had been vaccinated imperfectly—one in one place only, and the other in but two places.

The following important table is a classified summary of 2361 cases of small-pox treated during 1893 in the hospital ships of the Metropolitan Asylums Board:—

Character of Vaccination.	Cases of Small-pox.		Totals.		
	Discrete.	Confluent.	Cases.	Deaths.	Percentage of Deaths to Cases.
Under 10 years of age—					
Having scars of ½ sq. in. total area	21	0	21	0	...
„ between ½ and ⅓ sq. in. total area	12	2	14	0	...
„ less than ⅓ sq. in. „	19	0	19	0	...
„ unrecorded area	2	0	2	0	...
Over 10 years of age—					
Having scars of ½ sq. in. total area	794	30	824	17	2·06
„ between ½ and ⅓ sq. in. total area	215	13	228	6	2·6
„ less than ¼ sq. in. „	345	21	366	12	3·2
„ unrecorded area	128	12	140	7	5
Total vaccinated, under 10 years	54	2	56	0	...
Total vaccinated, over 10 years	1482	76	1558	42	2·6
Evidence of vaccination inconclusive, under 10 years	10	9	19	6	31·5
Evidence of vaccination inconclusive, over 10 years	173	58	231	38	16·0
No evidence of vaccination, under 10 years	217	65	282	63	22·3
No evidence of vaccination, over 10 years	140	75	215	31	14·4

We gather from the above table that "efficient" vaccination, as prescribed by the Local Government Board, not only confers on children under ten years of age an immunity from death by small-pox, which may be looked upon as absolute, but that the immunity thus acquired extends in the vast majority of cases for a much longer period; that in children, both over as well as under ten years of age, the more "efficient" the vaccination the milder the disease; that in unvaccinated children the virulence of the disease and its mortality are still as in pre-vaccination times; and that—taking into consideration other facts already noted relating to revaccination—if children over ten years of age are to enjoy similar immunity to that of their well-vaccinated juniors, "efficient" revaccination must be performed at puberty, or, better still, before it. Unfortunately, parents will always be found who object at first to more than "one mark" on the arm, and to prefer those doctors who will yield to their whim and "not hurt their babies." There are many medical men in practice who are ready to fall in with this foolish request, on the ground that half-protection will be better than none at all. But, in face of the experiences a few of which have been referred to already, medical men would do well to refuse absolutely to perform anything but vaccination of the most efficient sort. If a firm, united stand of this kind were made against the foolish prejudices of ignorant mothers, cases of post-vaccinal small-pox would be practically abolished amongst children, and would become much more rare amongst adults. Such a result could not fail to break down utterly the opposition to vaccination.

Sanitation and small-pox.—It is both interesting and instructive to examine some of the main arguments advanced by antivaccinators in their efforts to explain away the accumulating mass of statistical evidence of the value of vaccination. Those arguments, being oftentimes very plausible and arrived at by neglect or suppression of important considerations, have, unfortunately for the community, already misled a large number of worthy people who are not ready or able to make a study of the subject.

Thus we are seriously asked by Dr. A. R. Wallace and others to regard the fact that the small-pox mortality in this country has fallen enormously since the introduction of vaccination, as merely a "casual coincidence." The improved sanitation of modern times; the change for the better which has taken place in our habits as a nation; the introduction of a much larger supply of fresh vegetables and fruit; the extended "use of tea and coffee"; the better drainage and more cleanliness—these and such like beneficial influences are held up as the real enemies of small-pox. But, as Dr. M'Vail well puts it, "the group of agencies to which in the present day the adjective *sanitary* is usually applied—such as improved water-supply, improved excremental removal, increased living room, and better ventilation—have had their effect less in zymotics as a whole than in particular diseases, like cholera, enteric fever, and typhus, the causes of which lie in the particular evils that these agencies are fitted to combat. At the same time, it has been agreed that all that makes for cleanliness in eating and drinking and breathing has a good influence over all the diseases that trouble the human body, whether zymotic, constitutional, or local; and upon small-pox among the rest. Of the particular agencies which have been mentioned, increased living room and purity of air have the most effect against small-pox. But the ventilation which will extinguish a disease like typhus, whose virus cannot travel through more than a few feet of pure air, must have much less effect on variola, whose influence may extend for a quarter of a mile or more from an hospital in which its cases are congregated. Again, there is another and indisputable fact which the opponents of vaccination continually ignore: we have it on the Registrar-General's authority that, whilst the general death-rate in this country has decreased 9 per cent, that of small-pox has fallen as much as 72 per cent; and, furthermore, the decline in the small-pox mortality has been entirely limited to persons under fifteen years of age; there being actually an increase at every age above fifteen years. It is impossible, with any degree of consistency, to attribute this marvellous change in the age-incidence of small-pox to improvements in sanitation, by which all ages alike are affected. We find no such changed incidence in the case of the "filth diseases," properly so-called, which have long been proved to be amenable to good hygiene. The decrease in fever mortality has been common to all age periods; it has not been restricted to children. Further, if we take those diseases—scarlet fever, measles, whooping-cough—which are favoured by conditions that also favour small-pox, we find that, unlike the latter, the share of the mortality which is borne by children is the same now as it was half a century ago. In the case of no other disease has there been such a lessened incidence on children at the vaccination age as in the case of small-pox. Apart from vaccination there is no reason why small-pox should be affected to a greater extent by sanitation than, say, measles or whooping-cough. Yet during the same period that small-pox mortality has declined 72 per cent, that of measles has fallen only 9 per cent, and that of whooping-cough little more than 1 per cent.

It is a truism that all unwholesome conditions, all circumstances which lower the vitality of the individual, operate for evil and retard the recovery of the sick; and in the case of those infections, such as small-pox and scarlet fever, which are aerially conveyed, overcrowding would specially tend to spread an epidemic. An instance of this was furnished in the report of the Walsall epidemic of 1893. But, this condition apart, it is contrary to the experience of all competent observers throughout the world that small-pox should be affected materially by sanitary conditions. Very direct evidence on this point is to be found in some of the reports of recent outbreaks. Thus, Dr. Ainley, the Health Officer of Halifax, reports that, during the epidemic in that town in 1892-3, special record was kept of the sanitary condition of every house in which the disease occurred; 56·7 per cent of the houses were found in a cleanly condition; 29·4 per cent were in a fair state, and only 11·1 per cent were dirty: or, in other words, upwards of half of the invaded houses were clean and sanitary, nearly a third were very fair, and only a ninth were dirty. Dr. Niven, again, reports that in Oldham, during the epidemic of 1892, the disease mainly occurred amongst the better class of artisans, and singularly spared the worst parts of the town. That was, no doubt, in a great measure an accident, for it was not so in the previous epidemic; but what occurred in 1892 shows the fallacy of the contention that small-pox is a "filth disease" in the true sense of that term. At Warrington, according to the official report, "there is a great deal of bad property, dating from the period when the place was remarkable for the large population stowed away in a very small area, and was notoriously unhealthy." Yet it was observed during the small-pox epidemic of 1892-3 that the disease showed no special prevalence in those parts. Further, by referring to the figures for the Warrington epidemic, it will be found that the attack-rate amongst the vaccinated was 23; whilst the corresponding rate for the unvaccinated was 56. Amongst vaccinated children under ten 4·4 per cent were attacked, and 6 per cent died; whilst of the unvaccinated children of the same age-period the attack-rate was 54·5 per cent, and the death-rate 37·5. These facts are totally inconsistent with the opinion that sanitation governs the distribution of small-pox; for here it is clearly seen that, of a mixed population of vaccinated and unvaccinated persons, in invaded houses in the same area, exposed to precisely the same sanitary conditions, the incidence of the disease was vastly heavier upon the unvaccinated than upon the vaccinated. On the question of sanitation Leicester also furnishes evidence. During the last epidemic a particular group of fifty-four houses had their drainage arrangements individually examined by the smoke test; nine of these fifty-four houses were invaded by small-pox, and although four of these showed some sanitary defects, five of them exhibited none. The remaining forty-five houses were not invaded by small-pox, and yet nine of them showed sanitary defects.

The division into vaccinated and unvaccinated.—Another anti-vaccination argument is that the separation of the vaccinated from the unvaccinated is not a fair system of classification; to use Dr. Wallace's description to the Royal Commission (Q. 7421), "The unvaccinated would be necessarily to a very large extent of the very lowest class, including the tramps and the criminal classes, and also children who were too delicate to be vaccinated, and children who got small-pox before they were vaccinated." Much the same point was urged by Mr. Wheeler, who, referring to the difference in the mortality amongst the vaccinated and the unvaccinated, said he "should expect the vaccinated to come off better in cases of small-pox than the unvaccinated," and that "he should be. surprised if they did not, because they are a selected population; whereas the unvaccinated include the whole of the poor children who are rejected as unfit for vaccination, and they include all the postponed, because, being not totally unfit, they are to a certain extent unfit, and those form a considerable portion of a minority of the population—of a small minority, according to the Government account."

Now, what does this very ingenious way of trying to account for a remarkable set of facts amount to? Simply to this. If the unvaccinated are such a feeble, sickly set, they ought to suffer from infectious diseases other than small-pox to a far greater extent than the vaccinated. But no evidence of anything of the kind is forthcoming. When Mr. Wheeler was asked to furnish some evidence in favour of his assertions, he bravely referred to the *Sheffield Report;* and, on being pressed further, "opened it at page 48." But, so far from supporting Mr. Wheeler's contention, that page shows that out of 22 fatal cases of small-pox (20 of whom had never been vaccinated, 1 had been vaccinated only one day, and the other only five days before the appearance of the small-pox eruption), the previous health of 1 is recorded as "very good," of 12 as "good," and of only 5 as "delicate." In only 3 of the cases had ill-health been the cause of the neglect of vaccination. Six of the cases were under one year, and 7 under ten years of age. On pages 198 and 199 of his report, Dr. Barry has summarised the results of his personal inquiry into the fatal cases of small-pox which occurred in Sheffield during 1887 and the first three months of 1888; he there shows that out of 246 deaths amongst the vaccinated class, the previous health of the deceased was satisfactory in 129 instances, and unsatisfactory in 79 cases; whilst out of 343 deaths amongst the unvaccinated class, the previous health of the deceased was satisfactory in 210 cases, and unsatisfactory in only 77. In only 52 of the 343 fatal unvaccinated had "ill-health" been given as the reason for non-vaccination. It is needless to remark that if these are the kind of facts upon which Mr. Wheeler's argument is based, it falls to the ground.

Dr. Wallace, in support of his assertion, appealed to "the celebrated statistics of Dr. Keller," being evidently unaware that those "celebrated" statistics had already been exposed as false and partly fabricated. The statistics in question, which for a long time formed one of the stock weapons of the antivaccination armoury, related to some 60,000 officials and workmen employed on the Austrian state railways. As set out by Dr. Keller, they told strongly and strangely against vaccination. But the result was so extraordinary, and so totally contrary to all other experience, that Keller's figures were looked upon with suspicion from the very first. Indeed, when Keller was mentioned as an authority during the discussion on the Imperial Vaccination Law in the German Reichstag in 1874, Dr. Zinn, a member of the House, made the following remarks:—"Keller belongs to those who deny the existence of rabies and syphilis. In this he differs from his friends, who consider syphilis to be a consequence of vaccination. According to him, syphilis is nothing more than hydrargyria, a mercurial disease. You will discover how much trust is to be placed on these statements from the following facts, which I feel it my duty to disclose now that this authority has been quoted here. . . . A few years ago he published a pamphlet in which he stated that he had visited various looking-glass factories in Bohemia. He then gives the minutest details of the various symptoms which he observed amongst the populace—symptoms which, in fact, are thoroughly identical with those which appear in the course of syphilis. Now, the medical profession are not so credulous as to accept unsupported assertions, and, consequently, an extremely conscientious observer and scientist, Professor Bäumler of Erlangen, travelled through these remote districts so as to control Keller's statements, and found that those statements were partly superficial, partly inaccurate, and were, almost without exception, made in such an artful manner as to evade contention; he found that even the names of the places and their distances were not correctly given." Still, in spite of Keller's notorious untrustworthiness, it was not until 1887 that his statistics were thoroughly exposed. In that year Herr Körösi of Buda Pesth found that Keller had directly falsified the returns originally supplied to him by the railway surgeons, so as to serve his own antivaccination ends; figures being deliberately altered—such as 68 to 38. At the International Medical Congress at Washington in 1887 a committee was formed to examine into the matter thoroughly, and it eventually reported that all the returns submitted to them were, without exception, "falsified in such a manner as to raise the mortality from small-pox amongst the vaccinated, while that of the unvaccinated was lessened." These statistics are certainly "celebrated," but in a sense very different from that which Dr. Wallace meant when he so confidently referred to them.

The alleged risks connected with vaccination are carefully considered in a later section of this article. If half the contentions of the antivaccinators as to vaccination itself being the "cause of disease and death" could be maintained, there would be much justification for the position they have taken up. In that case, however, there would have been no necessity for the crusade, for the practice would not have been countenanced by the medical profession. In dealing with the risks of vaccination there is always one little item which vaccinators may well bear in mind, an item which is carefully avoided by antivaccinists; to wit, the healthiness of the German army. The German soldier of to-day is, without doubt, the "most vaccinated" man going, but he is at the same time the healthiest unit in modern armaments. According to antivaccinators the German army should be rotten with disease.

The evidence in favour of vaccination has been by no means exhausted in the foregoing pages; but sufficient has been said to show the overwhelming nature of this evidence in favour of the practice, and the comparative thinness as well as the frequent untrustworthiness and exaggeration of the arguments put forward on the other side. Speaking broadly, it has been shown that, taking the whole population, small-pox is no longer the scourge of infancy that it formerly was; but it has at the same time been demonstrated that the unvaccinated children of to-day suffer in the presence of an epidemic as severely as such children ever did, and that the decrease both of attack and mortality is confined to the vaccinated. It has been shown that efficient infantile vaccination protects almost absolutely from death and from severe attack, and, with comparatively few exceptions, from small-pox in any degree, during the first ten years or so of life; but that after that age its protective property gradually wears off unless the vaccination be efficiently repeated. It will be shown presently that, notwithstanding the gross exaggerations and distortions of the antivaccinators, the risks attending vaccination properly performed when compared with the gigantic saving of life, health and beauty which vaccination has effected, are so infinitesimal that they may be disregarded; excepting so far as they should accentuate the care to be taken by medical men in performing the operation.

It is urged by some people, with a show of plausibility, that, however beneficial vaccination may be, to have it generally compulsory is an intolerable infringement of the liberty of the subject. Such people, however, overlook the fact that the proved benefits of vaccination affect especially the helpless infantile portion of the community which has as yet no voice in the matter; and that the person who neglects to avail himself of the means of protecting himself against small-pox is a serious menace, nuisance and indirect cause of expense to the community in which he resides. Others, again, think that, as in the "Leicester system," the proper substitute for vaccination is compulsory "quarantine" for ten or twelve days; forgetting apparently that even Leicester, the parent of this system, finds it absolutely necessary, not only to protect its small-pox hospital staff by vaccination, but also to enforce, as far as possible, the vaccination or revaccination of all persons who may have been exposed to the infection. Most people, after looking seriously at the question, will agree that a quarantine of ten or twelve days is a form of compulsion vastly more costly, dangerous, "leaky," and individually irksome than that of vaccination.

Ernest Hart.

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E. H.

FOOT-AND-MOUTH DISEASE

SYNONYM.—*Aphtha epizootica.*

FOOT-AND-MOUTH disease is an acute febrile affection characterised by the formation of a vesicular eruption, the most constant seats of which are the buccal mucous membrane and the skin of the digits. It is highly contagious among ruminant animals, wild and domestic, and among pigs. It is frequently transmitted from these animals to human beings, and occasionally also to horses, dogs, cats and fowls.

History.—Although there is good reason to believe that foot-and-mouth disease was unknown in this country before the present century, it appears to have prevailed at intervals in the epizootic form in Eastern Europe for centuries before its introduction into Great Britain. In the sixteenth century it was described by the Italian writers Fracastori, Ruini, and Francisi; and in 1686 and 1687 it spread over Germany and France. In the following century it appears to have had a wide distribution over the continent of Europe, and numerous epizootic outbreaks of it are recorded. In the early part of the present century it was equally prevalent in Eastern and Middle Europe, but it was not till 1839 that the disease obtained a footing in Great Britain. The precise circumstances of its introduction here are not known, but during that year it speedily acquired epizootic dimensions among British cattle. The earliest reference to it in veterinary literature is found in the *Veterinarian* for 1839 (p. 639), where, under the heading, "The present Epidemic among Cattle," Mr. Hill, a veterinary surgeon of Islington Green, describes an outbreak in a dairy of 700 cows. Six of the cows were suddenly attacked "with a singular disease, the symptoms of which were precisely the same in each. The lining membrane of the whole of the mouth was in a state of inflammation and vesication. The tongue was involved, but the most extensive and annoying vesication was between the under lip and the gums. In two of the six it extended over the muzzle to the nostrils . . . and peculiar symptoms accompanied this—a continual catching up and shaking of one or other of the hind legs." These symptoms were at first attributed to some poisonous herbage; but that the disease was epizootic was soon made manifest, for in the course of about ten days more than 500 of the cows had been attacked.

Succeeding numbers of the *Veterinarian* contain other reports regarding the "Epidemic," the contagious character of which was soon recognised, although the possibility of its originating under "atmospheric agency" was entertained by many veterinary surgeons. Indeed, as late as 1857, Professor Simonds, in an article published in the *Journal of the Royal Agricultural Society* (vol. xviii. p. 201), denied that foot-and-mouth disease was imported; and for many years afterwards this opinion was used to combat the efforts of those who held that the disease never originated spontaneously, and ought to be opposed by measures calculated to stamp it out.

From the period of its introduction till 1866 foot-and-mouth disease was never absent from Great Britain; but by the end of the latter year, apparently owing to the operation of the measures directed against cattle plague, this country was nearly free from the disease. The next few years, however, saw an alarming recrudescence of the plague; and in 1870 and 1871 over a million animals were reported to have been attacked by it. The Contagious Diseases (Animals) Act came into force in 1878, and the repressive measures which it introduced had almost eradicated foot-and-mouth disease by the end of the following year. Unfortunately, during 1880 it began again to spread; and in 1883 nearly half a million animals were reported to have been attacked. After that date it gradually declined, until in 1886 only one outbreak was reported. For the following six years the British Islands were free from foot-and-mouth disease; but in February 1892 the disease was discovered among some Danish oxen in the Metropolitan Cattle Market. Notwithstanding the utmost vigilance of the Board of Agriculture this proved the starting-point of an epizootic during which, in England and Scotland, 5267 animals were attacked. Rigorous isolation, supplemented in some cases by slaughter of the affected animals and of those that had been exposed to the contagion, had the effect of exterminating the disease by the month of June 1892.

Since 1892 the importation of live cattle from countries in which foot-and-mouth disease exists has been prohibited; but, nevertheless, two isolated outbreaks occurred since the restriction was imposed, namely, one on the 1st January 1893, in a London cow-house, and another on the 17th February 1893, near Hastings. The London outbreak was suppressed by the prompt slaughter of all the cattle on the premises; and in the Hastings outbreak strict isolation sufficed to prevent the spread of the disease. In neither of these outbreaks was the source of the contagion traced; and it is impossible to say whether they were caused by virus that had lain dormant from the 1892 outbreak, or by virus brought from the Continent in imported straw, hay or hides, or adhering to the clothes or bodies of human beings.

Etiology.—Foot-and-mouth disease is an eminently infectious malady, and its history indicates that it belongs to the class of infectious diseases as opposed to the miasmatic. In other words, the germ or virus of foot-and-mouth disease does not propagate itself save in the bodies of affected animals; every case of the disease is ascribable to germs derived from an antecedent case. In the vast majority of cases searching inquiry suffices to bring the source of the contagion to light; and the exceptions to this rule in no way compel us to admit that the disease is ever due to spontaneous development or miasmatic poison; since it is known that the virus of the disease possesses considerable vitality outside the body, and, adhering to inanimate objects, may be carried long distances in an active condition. Fresh outbreaks, without actual contact between animal and animal, may thus be brought about by such means as farm-yard manure, straw, hay, railway waggons, steamboats, human clothing, and so forth. Many instances have been observed in which the clothes of milkmaids or other farm-servants have transported the virus of the disease from one locality to another. It is probable also that wild animals, such as rooks, hares, and rabbits, although not themselves affected, may transport saliva of infected animals from one field to another, and thus spread the disease.

There can be little doubt that at a certain stage of the disease the causal germs are carried by the circulating blood; though in general the disease cannot be transmitted by inoculation with that fluid in moderate quantity. On the other hand, the agent of infection appears to be always abundantly present in the fluid of the vesicles which form in the mucous membranes or skin, and in the discharge from the ulcers left by those vesicles when they burst. The buccal saliva is highly charged with the virus from the first appearance of the eruption in the mouth; but there is no reason to believe that the agents of infection are excreted by the salivary glands. In like manner the milk is probably not infective except when soiled with the contents of vesicles that have formed on the exterior of the teats or in the interior of the gland, or by the hand of the milkmaid.

To what extent the virus may be carried by the air is unknown. The older writers on the subject regarded the virus of foot-and-mouth disease as belonging to the class of *fluid contagia*, and many believed that it could be carried for miles in the atmosphere. For example, the rapid spread of the disease over nearly the whole continent of Europe in 1839, and even across the sea to England, was regarded by Haubner as conclusive evidence of the fluid nature of the virus; and it was asserted that the disease on that occasion broke out in the most isolated localities, such as mountain districts and forests, where there was no cattle traffic with the surrounding country. At the present day it is not necessary to combat the theory that the virus of foot-and-mouth disease is gaseous in its nature; and the history of the most recent European outbreaks proves that the sea is a very efficient barrier to the spread of the disease. From 1892 to 1894 the continent of Europe was ravaged by foot-and-mouth disease; but, since the importation of animals from infected countries was prohibited, Great Britain has been free from the disease, save for the two isolated outbreaks at London and Hastings in 1893.

In illustration of the ease with which the infection of this disease may be spread by intermediary bearers, the following case may be quoted:—Gensert, a German veterinary surgeon, visited a byre in which foot-and-mouth disease existed, and remained in it for about ten minutes. Two hours afterwards, having changed his hat and coat, and washed his hands with soap and water, he started to make another visit, and drove for an hour and a half in an open conveyance. Having arrived at his destination he performed an operation on the eye of a cow. Eight days afterwards the cow showed symptoms of foot-and-mouth disease, and within a few days all the other cattle on the premises were affected. This was the first outbreak in the neighbourhood, and Gensert, therefore, had no doubt that he had carried the contagium on his clothes.

In the preceding paragraphs the terms virus and contagium have been used to designate the causal agent of foot-and-mouth disease, but the exact nature and form of this agent are still matters of dispute.

Bacteriology.—Dr. Klein, as the result of investigations made in 1885, regards a micrococcus which he found in the vesicles in sheep as the cause of the disease. This organism occurred singly in the fluid of the vesicles, in dumb-bells, and in chains; it stained well with the ordinary aniline dyes, and it was easily cultivated in milk, bouillon, gelatine, and agar. Klein described his own investigations as fulfilling "all the conditions required for a demonstration of the causal connection between a given micro-organism and a given infectious disease; namely, demonstration of the organism in the diseased tissues of the animal body affected with the malady; successive subculture of the demonstrated organism many times repeated outside the animal body; successful production in another animal body of the identical malady by administration to it of the organism of such subcultures; and identification in the diseased tissues of that artificially induced malady of the very same organism which had been in the first instance associated with the given infectious disease." Notwithstanding numerous subsequent investigations by competent bacteriologists, Dr. Klein's discovery remains uncorroborated; and we are therefore almost driven to conclude that the streptococcus found in the vesicles of the sheep was an accidental impurity, and that the experimental sheep were not infected by the culture of this streptococcus, but by the natural virus accidentally conveyed to them.

Schottelius found in the contents of foot-and-mouth vesicles peculiar bodies which he named streptocytes. They were round in shape, and united in longer or shorter chains, the terminal elements of which sometimes showed projections like the pseudopodia of amœba. Some of the elements appeared to be dividing in the direction of the long axis of the chain. No growth took place in artificial media below 37° C. In hanging-drop cultures the streptocytes formed shorter chains, and were mobile; but no cilia could be demonstrated. The organisms did not stain well with methylene blue, but they took the colour of gentian violet well, and were stainable by Gram's method. Febrile symptoms were excited in calves and young cattle by inoculation with the cultures, but experiments with sheep and pigs had a negative result.

In 1893 Behla found in the blood of animals suffering from foot-and-mouth disease structures which, he thought, were possibly identical with the streptocytes of Schottelius; and in the same year Kurth, working in the German Imperial Office of Health, found as the most frequent organism in the vesicles a streptococcus which had peculiar characters when cultivated in bouillon to which liquid blood serum had been added. Kurth named the organism the Streptococcus involutus, and he was inclined to regard it as the causal agent of foot-and-mouth disease, although all attempts to reproduce the disease with artificial cultures failed.

In 1893 the Prussian Minister for Agriculture offered a prize of 3000 marks for the discovery of the cause of foot-and-mouth disease, the stipulation being made that claimants of the prize must not only indicate the agent of infection, but must also be prepared to demonstrate its pathogenetic properties by experiments on animals.

The first **symptoms** generally appear from one to eight days after infection. In cattle these are slight dulness, shivering, loss of appetite, "staring of the coat," and stiffness in movement. If the temperature be taken at the time it will be found already two or three degrees above the normal. Within a few hours these premonitory symptoms of illness are followed by others which are characteristic of the disease. The animal ceases to feed, and is reluctant to move; from time to time it makes a peculiar smacking noise with its lips, from which a more or less frothy saliva escapes. If the mouth be opened, white blister-like elevations will now be found on some part of the buccal mucous membrane; these soon burst and become converted into shallow erosions. When made to move, the animal is obviously lame or "tender on its feet"; and while standing it frequently shifts the weight from one leg to the other, and shakes its feet as if to get rid of something adhering to them. This tenderness of the feet is well marked even before the formation of vesicles; but these soon appear on the interdigital skin, or on the posterior aspect of the hoof immediately above the horn.

When the buccal vesicles have burst, the animal suffers increased pain in the mouth, rumination is entirely suspended, and all food is for a time refused; in consequence of reflex irritation there is a copious secretion of saliva, much of which, owing to the pain of deglutition, is allowed to trickle from the mouth. The general appearance of the animal is now indicative of great depression—the eyes are dull, the ears drooping, the back arched, and the hair erect and lustreless. The bowels are generally more or less constipated, and in milch cows the secretion of milk is greatly diminished or almost arrested.

These symptoms in moderate cases last with little or no amelioration for nearly a week, during which time the animal rapidly loses condition. At the end of that time the fever begins to subside, and the pangs of hunger compel it to attempt mastication if succulent grass or other soft food is to be had. The tenderness of the feet gradually declines also, and in uncomplicated cases of moderate severity all the visible symptoms of the disease have disappeared within ten or fourteen days after the onset. In young animals, liberally fed, the former good condition is usually rapidly reacquired after an attack of foot-and-mouth disease; but complete recovery is much slower in older animals, and particularly in milch cows.

The symptoms in sheep are generally somewhat different from those just described, inasmuch as in them the mouth lesions are frequently slight, while those of the feet are constant and severe. Thus the chief symptom is great lameness, associated at the outset with suspension of rumination, refusal of food, and febrile disturbance. The pain in the feet is so great that the animal is unable to gather its food, and lies persistently, with consequent rapid loss of condition. The lesions in the feet are much aggravated if the sheep are driven long distances on hard roads, and in such circumstances "casting of the hoof" frequently results.

In pigs, as in sheep, the feet symptoms predominate. The animals lie persistently in their litter, and when forced to move they frequently squeal from the pain in their feet.

Pathological anatomy.—The characteristic lesion of foot-and-mouth disease is a vesicular eruption; and, as the name expresses, the feet and the mouth are the main seats of election of the eruption. In milch cows vesicles not infrequently form on the skin of the teats and udder; and occasionally the eruption appears in other situations, such as the muzzle, the nostrils, the skin of the vulva and perineum, or the mucous membrane of the throat, gullet, stomachs or intestines. The localisation of the lesions in the mouth or feet is in no way ascribable to the method of infection, though this has been asserted by some authors. Animals infected by way of the alimentary canal may have an eruption on the feet as well as in the mouth; and an eruption in both of these situations may follow infection by inoculation at any part of the body.

In the mouth the vesicles may form on any part of the mucous membrane; but they occur most frequently on the inside of the lips, the pad of the upper jaw, and the tongue. Their appearance in these situations is no doubt preceded by a stage of inflammatory hyperæmia, but this is seldom noticeable owing to the thickness of the epithelium. The stage of vesiculation is determined by the escape of a thin serous exudate from the vessels of the inflamed corium, and its accumulation in the deeper layers of the epithelium. Small cavities containing a clear liquid are thus formed in the rete Malpighii, and these gradually increase in size and become confluent, while the stratum corneum becomes stretched and upheaved into a blister-like elevation. The bursting of the vesicle is hastened by the movements of the tongue or lip, and the vesicle becomes converted into a shallow erosion or ulcer, the bright red floor of which is formed by the congested papillæ of the propria mucosæ. The vesicles vary in size from a sixpence to a five-shilling piece, and their outline may be circular, oval, or irregular. In uncomplicated cases regeneration of the lost epithelium promptly sets in, but this is always retarded by the movements of the tongue and lips, and by the presence of adventitious organisms in the mouth.

In other situations the histology of the lesions is essentially the same as that of the buccal eruption. In the feet also the access of other microbes tends to aggravate the inflammation, which may extend to the whole vascular corium and lead to complete detachment of the hoof.

Transmissibility to Man.—That the human subject may contract foot-and-mouth disease is proved by many well-attested cases, of which a few may here be cited.

As early as 1834 three German veterinary surgeons made themselves the subjects of an experiment by drinking the milk from cows affected with foot-and-mouth disease. Each of them consumed about a quart of milk, and on the second day of the experiment premonitory symptoms, in the shape of fever, headache, and itching of the hands and fingers, were manifested in one of them. Five days later a vesicular eruption formed on the mucous membrane of the tongue, cheeks and lips, and on the skin of the hands and fingers. The other two experimenters were similarly attacked, save that the eruption was confined to the mouth.

In this country numerous cases of the transmission of the disease were noted by veterinary surgeons during the first few years after its introduction. In most of these cases infection took place by means of milk from affected cows, but instances of infection by inoculation were also observed. One of the most interesting of these is recorded in the *Veterinarian* for 1831 (p. 152). The patient was a farmer who had injured one of his fingers in drenching a cow suffering from foot-and-mouth disease. The wound took on an unhealthy action, and after some days he was taken ill with a cold shivering fit. This occurred in the evening, and by the following morning the cold fit had been succeeded by fever. Twenty-four hours later an offensive discharge from the nose set in, and vesicles formed on the gums and tongue.

In the same journal for 1842 (p. 93), a correspondent states that himself and all his family and domestics were attacked on the lips and in the mouth in consequence of using the milk of his diseased cows.

During the German epizootic of 1892 very numerous instances of transmission of the disease to human beings by means of milk were reported. In a considerable number of cases milkmaids contracted the disease through inoculation of the hands in the act of milking; and in one such instance vesicles formed on the breasts as well as on the hands. Many persons who had to handle or attend to diseased cattle contracted the affection by bringing their dirty fingers into contact with the lips. A shepherd was infected by holding in his mouth the knife which he had used to pare the feet of diseased sheep. A veterinary surgeon who contracted the disease had from 30 to 40 vesicles on his hands; and a workman who had to dress the feet of diseased cows had, besides an extensive eruption on both hands, a severe inflammation of the conjunctivæ. A child of a year old, which had consumed milk from diseased cows, sickened with fever and gastric disturbance, followed by the formation of vesicles on lips and tongue and between the fingers and toes.

Professor Clifford Allbutt informs me that during the epidemic of 1883 he was called to a country house in Yorkshire to see three sick children, in whom he was able at once to diagnose foot-and-mouth disease. The disease, so far as he remembers, was in the mouths of the patients only, but he did not see the patients again. The presence of this disease in the district was ascertained, and the milk consumed by the children came from neighbouring farms, where ample sources of infection existed. He heard that the children made a good recovery. After the diagnosis of these cases some others were reported to him by medical men in the same district. All seemed to be of a comparatively mild character.

The following two cases show that the virus may retain its activity in butter :—

On the 18th of November 1890 a veterinary student in Berlin had sent to him by his brother-in-law a packet of fresh butter made from the milk of cows suffering from foot-and-mouth disease. On the following day he ate some of the butter for the first time. During the next night he was feverish, and on the morning of the 10th he found his under lip red, swollen, and completely covered with vesicles as far as the chin. The vesicles were somewhat itchy. Subsequently vesicles formed on the tongue and on the right ear. During the first eight days the parotid and sublingual salivary glands were slightly swollen, and the amount of the salivary secretion was increased.

In 1892 a German clergyman became affected after consuming butter made from the milk of his own cows, which were suffering at the time from foot-and-mouth disease. The disease was ushered in by slight rigors, diarrhœa, and itchiness of the skin ; and on the third day numerous vesicles formed in the mouth, and on the face, neck, breast, and arms. The eruption had healed up at the end of ten days.

It is not improbable that some outbreaks of so-called "stomatitis epidemica" in mankind may turn out to be foot-and-mouth disease ; and in all cases of such a character careful inquiry should be made into the possibility of the infection.

J. M'Fadyean.

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J. M'F.

RABIES

Synonyms.—*Hydrophobia* (in man only) ; Gk. and Lat. *Lyssa* ;
Fr. *La rage* ; Germ. *Hundswuth*, *Wassenscheu*, *Tollwuth*.

Rabies, like glanders, is a disease usually contracted by man through infection from one of the lower animals. It is then associated with an injury, such as the bite of a dog, and the inoculation of the broken surface with the saliva of an animal affected with declared or latent rabies. This is the so-called rabies of the streets : wolves, cats, foxes, and dogs ; horses, cows, and deer may contract the disease: monkeys, rabbits, and guinea-pigs are all inoculable with it, as indeed are all warm-blooded animals.

A much larger proportion of men and children are affected with hydrophobia than of women; this is undoubtedly because the latter, both from their mode of life and from the nature of their clothing, are much less exposed to the attacks of rabid dogs.

In Great Britain and Ireland the disease is confined among animals almost entirely to the carnivora; and though somewhat rife in Ireland, England, and Scotland, it is found only in certain districts.

In 1893, 94 cases occurred in eighteen counties of England and Scotland; whilst in 1894 no fewer than 248 cases of rabies in dogs were reported; and in 1895, 672 cases. In addition to these cases, 55 other animals, including 5 cats, were attacked with rabies. In 1893, 46 of these cases came from Scotland; in 1894, 29; and in 1895, 4 only.

Most cases occur in Lancashire (130) and in Yorkshire, especially the West Riding with its 308 rabid dogs and 30 other animals, including 5 cats; then follows at a long interval Cheshire (31 cases); and then come London, the "Home" counties, Ayrshire, Lanarkshire, Edinburgh (45 cases), Dumbartonshire, Hants, Essex, Cornwall, Stafford, Durham, Northumberland, Cumberland, Derbyshire, Northampton, Warwickshire, Lincolnshire, Notts, Salop, and Hereford.

In the metropolitan district, in which the muzzling order is now in force, there were in 1889 no fewer than 176 cases; in 1890 the number of cases had fallen to 44, in 1891 to 28, and in 1892 to 3; this fall corresponded and was continuous with the enforcing of the muzzling order. As soon as the order was allowed to lapse, a rise in the number of cases began and continued until the order was reinforced. During the four years mentioned no fewer than twenty-five persons died of hydrophobia, and 147 cases were sent for treatment to the Pasteur Institute.

Incubation.—The first symptoms of rabies may follow inoculation after intervals of three weeks, six weeks, or twelve to eighteen months; fourteen days on the one hand, and two or even five years on the other, have been given as the extreme limits of the incubation period. This period seems to vary according to the susceptibility of the patient, the virulence of the disease in the animal inflicting the wound, the amount of virus introduced, and the position of the bite. Meanwhile there may be no symptoms of any kind, and the wound heals well with little local or general disturbance. At the end of the period of incubation the wound becomes uncomfortable; there is itching, tingling, and a sensation of local heat which may be almost unbearable; this is usually accompanied by a sharp, stinging pain which may be localised in the wound, or may follow the course of the nerves; sometimes the wound becomes livid or opens up afresh and assumes an unhealthy purulent appearance. This event is sometimes accompanied by an outbreak of small vesicles around the wound, or on each side of the tongue on its under surface (Marochetti), which may ulcerate. These are the only external anatomical lesions which have been described, and they occur but rarely.

Symptoms.—During the early stages the patient is feverish and very thirsty; he becomes exceeding depressed, anxious and irritable, and has a peculiar hunted look in his eyes; the muscles of the face are drawn and restless, and there is marked pallor. Mr. Makins, taking the description of Bristowe as his basis, well describes this stage. He says that the patient may talk freely, the sentences being sometimes interrupted by sighing inspiration; he usually shows great unwillingness to speak about the possible cause of his illness; sleep is often broken by dreams; the mouth is dry, the patient complains of thirst, and is disinclined to swallow; loss of appetite, nausea, and epigastric uneasiness and a general hyperæsthesia then come on; the pulse quickens, sometimes becoming very rapid, and the respirations are proportionately hurried and shallow. On the second or third day the patient becomes much more excited; he is restless and agitated; speaks disconnectedly, and may become slightly and intermittently delirious; he seldom fixes his eyes on anything, and is constantly giving suspicious side glances, as though on the outlook for some hidden danger; the pallor becomes more marked; the eyes are bright, and the conjunctiva, like the mucous membrane of the mouth and fauces, is markedly congested. On the congested mucous surfaces there is usually an accumulation of thick, tenacious mucus, and in his efforts to expel it the patient emits a harsh coughing sound, which is likened, not very aptly, but very naturally to the barking of a dog. Thirst is often a prominent symptom, yet along with this there is usually great difficulty in swallowing, especially fluids. At first the patient is anxious to drink, and he makes the most determined effort to do so; but the moment the fluid comes in contact with the fauces it is expelled with considerable violence, and violent spasmodic contractions of the muscles of deglutition and of ordinary and extraordinary respiration come on: this is often followed by a tetanic state, with marked opisthotonos and temporary cessation of respiration. The "tendon reflex" and skin reflexes are often markedly increased. These symptoms may abate, only to recur when another attempt is made to drink; or even on the stimulation of a sharp sound, a touch, a bright light, a breath of air, or the mere sound of water: ultimately indeed, after making one or two attempts to swallow fluid, the very sight of water causes such terror to the patient that he is anxious to avoid it. In some cases "sudden severe throat-spasms have been the first symptoms"; and attacks of vomiting often come on at this stage, greenish brown liquid being thrown up. The symptoms so noticeable in the dog —the desire to be alone, the suspicion of every movement, the surliness, alternating with periods of extreme excitement—are noticeable in the human subject also. The delirium as a rule is intermittent; the patient rambles, but can be brought back to consciousness and quietness by his attendants. During the early stages of the disease increased sexual desire is often a marked symptom, and in the later stages it becomes still more troublesome. The urine may contain sugar, albumin, or even blood. The repeated attacks, however, rapidly exhaust the patient, and if the disease be somewhat prolonged there may be great wasting. "The pulse becomes quick, irregular, and small in volume, and respiration quick and shallow, a deep inspiration often inducing a convulsive attack, tenacious mucus accumulates in the mouth and fauces, articulation is thick; later the convulsive attacks increase in frequency, and death from asphyxia may occur during one of them. In other cases the progress is slower, the eyes sink, the brow sweats, the lips become blue, and the patient dies of slow asphyxia, or occasionally an almost complete remission of convulsive attacks may precede death from exhaustion, the mind in other cases remaining clear to the end" (Makins). Sometimes a condition which corresponds to the dumb or paralytic rabies of animals is seen, in which the only symptoms are those of Landry's paralysis—an acute ascending paralysis beginning in the lower limbs, and gradually spreading upwards until the muscles of the neck and face are involved. This condition appears to be due to a later extension of the disease to the cord, except in those cases in which the poison from the rabid animal makes its way directly into the veins. It is probably for this reason that the dumb or paralytic form of the disease is so frequently met with in animals in which rabies has been produced experimentally.

Diagnosis.—The only diseases with which rabies may be confounded are hysteria, insanity, tetanus, and Landry's paralysis. The first of these can be discarded only after a careful study of the symptoms, and after eliminating the possibilities of infection by the bite of a rabid dog: where patients have been bitten by dogs that were not rabid, and have never manifested any signs of hydrophobia, the diagnosis can of course be settled at once; but in some cases where hysteria associates with mania, or great mental disturbance is met with, the diagnosis is often a matter of some difficulty, a difficulty, however, which as a rule does not extend beyond the fourth day of the disease: under these conditions the patient may (especially if fear of the result of a bite even from a non-rabid animal be the cause of the hysteria) bark and bite or snap almost continuously; but, as has frequently been pointed out, these patients do not suffer from the characteristic respiratory spasm, which is always accompanied by a peculiar catching of the breath said to be pathognomonic of rabies. Tetanus, which sometimes follows the bite of a dog, may be distinguished by the shorter incubation period, the tonicity of the spasms, and the contraction of the levatores anguli oris which gives the grinning expression peculiar to tetanus, and very different from the haggard, hunted look so characteristic of rabies; the marked rise of temperature that occurs in tetanus is also said to distinguish it sharply from hydrophobia, in which the temperature is never much raised, and may be normal or sub-normal. Dr. Gowers, writing on this latter point, maintains that this is not an accurate conclusion. He says: "At the outset the elevation is trifling (occasionally, indeed, absent), and throughout the disease it may remain moderate, 100° to 101°. More frequently, as the symptoms increase, so does the pyrexia, and it amounts to 103°, 104°, or 105°, and may even reach a still greater height just before death, and may continue to rise for a short time after death. A rectal temperature of 108·8° has been observed twenty minutes after death (Handford)." Diagnosis between hydrophobia and Landry's paralysis may be only possible after a careful study of the history of the attack has been made.

Rabies in the dog is very similar in its clinical history to hydrophobia in man, except that it does not take the form of hydrophobia; the animal loses its good temper and desire for human society, becomes morose and sullen, and hides under sofas and chairs, or in quiet corners; if at rest it snaps at anything that is presented to it, and even when undisturbed goes about snapping as if trying to catch flies: there is congestion of the mouth, tongue, and fauces, and marked salivation; the mucus is sticky and readily becomes frothy; the conjunctivæ become red; the animal will often run straight ahead, turning neither to the right nor to the left, but snapping at everything that comes in its way; depraved in appetite, it may swallow any kind of rubbish, so that after death small stones, hay and straw, hair, shavings, bits of wood, and the like, may be found in its stomach—the stomach in some cases being much distended: the animals do not avoid water, and in association with this fact it has also been noted that there is little or no cutaneous hyperæsthesia. The bark usually becomes changed into a peculiar howl, which begins with a short low note and ends with a long higher note; it has also a peculiar metallic ring (Gowers). Emaciation sets in, and in the later stages of the disease the hind limbs and the lower jaw, which drops, may be paralysed; other muscles may also be affected.

The method of diagnosis, used by Pasteur, of injecting small portions of the cord of the animal supposed to be rabid into the subdural space of a rabbit, although sometimes too late to guide us to use any special antirabic treatment, should invariably be resorted to if merely for the sake of reassuring the patient—especially if he be nervous, irritable or hysterical. The great and protracted mental strain after a dog-bite may often be very greatly relieved when the result is negative; if, on the other hand, positive results are obtained, the patient is no worse off than before, unless it be thought necessary to make him acquainted with the diagnosis. An inoculation should therefore be made in every case of suspected rabies, if the dog can be identified and secured. As yet these inoculations have to be made in private laboratories; and, partly on account of the outcry against the Pasteur treatment, and partly for other reasons, we have in this country no institute to take charge of the preparation of the Pasteur inoculating material, or to undertake in any way the treatment of patients bitten by rabid animals. We are now among the last of the nations to be unprovided with facilities for carrying on this method of treatment.

Prognosis.—The percentage of deaths of patients bitten by rabid dogs was given variously at from 5 to 50 per cent before the introduction of Pasteur's treatment.[1] The most trustworthy figures, however, are those which give the mortality at 16 per cent of those bitten by rabid animals. This percentage included practically all those in whom the symptoms of true hydrophobia appeared; that is, those cases were left out of account in which merely subjective pain and other phenomena were ascribed to the wound caused by the bite, and after which nothing more than hysterical symptoms supervened. When the symptoms are developed, the patient almost invariably succumbs within four days, sometimes after as short a period as twelve hours.

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[1] Böllenger states that from a series of collected statistics, it may be gathered that of all patients bitten by dogs undoubtedly rabid, 47 per cent suffer and die from hydrophobia.

Morbid Anatomy.—On autopsy the main features observed are fluidity of the blood, congestion of the fauces, larynx, trachea, lungs, pharynx, œsophagus, and stomach; and in the mucous membrane of the latter, according to Bristowe, hæmorrhages may be found. In the dog the teeth are often broken, and the tongue and buccal mucous membrane are lacerated and inflamed. There is also marked congestion of the central nervous system and the meninges; there may be acute meningitis with a distinct effusion of lymph and even minute hæmorrhages, and fluid in the ventricles is not of uncommon occurrence: small extravasations of blood have been noted in the spinal cord. On microscopic examination it is found that there is a migration of leucocytes into the perivascular lymphatic spaces and into the connective tissue of the nerve-centres. Microscopic hæmorrhages have also been found; these I have found, as pointed out by Gowers and others, specially well marked near the floor of the fourth ventricle; but according to Horsley they may occur at different points in the central nervous system, so that the whole must be examined. Congestion of the peripheral nerves and of the sympathetic system have also been described; and Coats and Elsenberg have pointed out that in some cases, in addition to the migration of leucocytes in the medulla oblongata, there is an accumulation of leucocytes in the salivary glands — especially in the parotid, in the mucous glands of the larynx, and in the kidneys; this condition being associated with the marked congestions that occur in these positions.

Clifford Allbutt, Gowers, Greenfield, Golgi, Gianturco, Schaffer, Babes, and others have written on the specific character of the lesions of the nervous system in cases of rabies.

Clifford Allbutt in 1872 described vascular congestion, hæmorrhages, transudation, thickening of the walls of the vessels, patches of nuclear proliferation and degeneration, and disappearance of nerve strands as occurring in the cerebrum, medulla oblongata, pons and spinal cord; and indicated that all these changes may be regarded as pointing "to the action of an animal poison acting primarily on the cerebro-spinal nervous system." He pointed out (1) that the order of severity of the pathological lesions was worst in the medulla; then follow in order the cord, the central convolutions, and, lastly, the central ganglia of the encephalon: whilst the order of symptoms during

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Where the wounds have not been cauterised, 83 per cent of the cases succumb; where they have been cauterised, in some cases not very promptly, 33 per cent die.

life, as he indicates, corresponds fairly definitely: "first, intense reflex irritability in the region of the medulla, with no tetanic symptoms and no delirium; secondly, increasing hyperæsthesia throughout the cord, with semi-tetanus; thirdly, delirium."

Gowers noted a granular appearance in many of the nerve-cells, and "adjacent to or around many cells were spaces, in some cases apparently empty, in others containing granules." He also noted the presence of pigment granules in some nerve-cells and of corpora amylacea. In some of the smaller vessels he found thrombi, and in the perivascular lymphatic sheaths he described numerous small cells or corpuscles which he looks upon as migrated leucocytes; these are so densely packed as to cause actual compression of the vessel. To some of these collections he gives the name of "miliary abscess." The lesions, he considers, are usually found in the region "in which experimental physiology has located the 'respiratory centre' of the medulla," and he says "it is of interest to note that the paroxysms of spasm which constitute the chief feature of the developed disease are paroxysms of respiratory spasm." He concludes that "there is certainly nothing in the histological characters of the lesions which can be regarded as specific of the disease. The collection of cells in the perivascular sheaths has been observed in other diseases . . . but the distribution of these lesions, their intensity in the lower part of the medulla and in the neighbourhood of certain nerve nuclei is, as far as I am aware, peculiar to the disease, and constitutes a distinguishing anatomical character."

Benedikt lays stress upon the appearance of hyaloid patches in and around the vessels. These are usually accompanied by miliary inflammatory foci similar to those described above. Several authors maintain, however, that these hyaline or hyaloid degenerations are found in similar positions in aged dogs and in various other diseased conditions.

Lüttkemüller found a moderate increase in the number of white blood corpuscles in the blood of rabid animals, accompanied by the presence of an extraordinary number of microcytes.

Germano and Capobianco have quite recently published further observations which confirm and extend those of previous investigators. Using the methods devised by Paladino, Golgi, Marchi, Weigert, and Pal, they find that the lesions described by Golgi, although not pathognomonic since they are undoubtedly found in other affections of the nerve-centres, are nevertheless (especially as regards their distributions) constant in the various forms in which they manifest themselves, from the simple hæmorrhage up to the destruction of nerve-cells and the marked hyperplasia of the neuroglia. Moreover, they find that these lesions are constant in character, in order of appearance, and in that they specially affect the motor tracts. In the spinal cord of rabid dogs and rabbits constant anatomical changes are found; but although all the elements of the nervous tissue are attacked, the lesions are not uniformly distributed in the various sections of the cord; the motor regions, as above noted, being specially affected by an acute inflammation of the nervous tissue, which results in degeneration of the nerve-cells and even in complete disappearance of this element; the neuroglia and the myeline sheath undergo simultaneous changes which apparently are in intimate association with one another. The small neuroglia corpuscles or cells become much larger and more visible than in the normal state. It appears, indeed, that in the myelitis set up in the cord in rabies, the irritant brings about the destruction of the nerve elements proper (cells and fibres); and that, following this or set up by it, is a hypertrophy or hyperplasia of the neuroglia, which probably leads to destruction and absorption of the cells and nerve-fibres.

Babes, in a paper published in October 1895, after noticing the congestions of various parts of the alimentary tract, describes very minutely the lesions found in the central nervous system, which he describes as falling into two groups: (i.) the more diffuse alterations leading towards general œdema and hyperæmia as a result of commencing inflammatory changes around the blood-vessels; (ii.) the more definite and localised changes; such as dilatation of blood-vessels and hæmorrhages in proximity to the central canal, in the floor of the fourth ventricle, especially immediately under the ependyma, and in various parts of the mucous and serous membranes. Changes take place in the walls of the vessels, hyaline patches appear in them, and they swell up and become more or less hyaline throughout, whilst the endothelium proliferates: these changes often lead to obliteration of the vessels, which appear to be surrounded by thick hyaline masses. The nerve-cells next suffer, swelling up distinctly, whilst small hyaline bodies, circumscribed by a pale zone or by vacuoles, make their appearance in the vicinity of the nucleus. Leucocytes fill up the pericellular space, crowding on the nerve-cells, whose nuclei ultimately disappear.

Babes, in opposition to the authors quoted above, regards these histological alterations as absolutely pathognomonic of rabies. For diagnostic purposes he takes a small piece of the spinal cord of the suspected animal, hardens it in alcohol for a day, then stains it with aniline red, and searches for the characteristic hyaline nodes (Wuthknötchen); he asserts that in this way he is able to obtain a rapid and definite result, and that he has never known the method to fail.

Etiology.—The poison, whatever may be its nature, is usually contained in the saliva; and as early as the beginning of this century experimental rabies was produced in the dog by inoculation with the saliva of a hydrophobic patient. The bulk of the toxic material appears to be excreted in the saliva of the parotid gland; though a certain smaller quantity may be excreted by the other salivary glands, and also by the lachrymal glands, the pancreas, and the mammæ of rabid animals: indeed, rabic symptoms may sometimes be induced by the inoculation of milk from affected animals. The poison may also be found in the suprarenal bodies, and in the fluid and substance of the cerebro-spinal nervous system, especially the medulla oblongata; it is found also in the peripheral nerves, though in much smaller quantities than in the central nervous system.

It was supposed at one time that it might be found in the blood; but such is not the case. The saliva of a dog has been found to contain the toxic material three days before the manifestation of the disease.

That the disease is due to some form of organism which has the power of multiplying in the tissues and of producing a toxic substance, which, as in the case of tetanus, appears to act specially upon the central nervous system, can now scarcely be doubted; but the exact nature of the poison has not yet been determined. As in other specific infective diseases the virus is transmitted directly from animal to animal through the medium of some fluid or secretion; it is now very generally recognised that the disease cannot arise anew as was at one time assumed. In rabies, again, as in other specific infective diseases, there is a period of incubation, during which the poison appears to increase in quantity; in which respect it is unlike snake-bite, where the symptoms come on with excessive rapidity. It has been concluded, therefore, that some organism capable of producing the poison must be concerned in the process: indeed, the whole history of a case of hydrophobia so much resembles a case of tetanus in its essential details, that, unlike as the two diseases are in certain respects, the demonstration of a microbic factor in the one naturally suggests a similar factor in the other. This factor, however, has not yet been satisfactorily demonstrated. Gibier, Pasteur, Chamberland, and Roux, Fol, Babes, Dowdeswell, and others, have from time to time described micrococci of various sizes, aerobic and anaerobic in their growth, presenting different appearances in cultures, and staining by different methods; but when it has come to a rigid proof of the causal connection of a particular organism with the disease the chain of evidence has invariably broken down at some critical point. Recently Dr. G. Memmo has announced that he has succeeded in obtaining pure cultures of a blastomyces from the brains of six rabbits that had succumbed to experimental rabies; and also from the brain of a four-year-old child which had died from hydrophobia set up by the bite of a mad dog. On culture media this organism grows slowly when first taken from the animal, but in succeeding generations its growth is much more luxuriant and definite. When found in the brain, the round cells of which it consists are indistinguishable from the various forms assumed by the myelin; especially when the brain is reduced to an emulsion. In cultures the cells are of various sizes; the smaller ones are round, the larger oval or round. They are stained by the aniline dyes (not by Gram's method). The organism grows best at the body temperature and is pathogenetic in animals. When inoculated intraperitoneally into guinea-pigs it causes, in from 11 to 20 days, a paresis of the hind limbs which rapidly increases in extent and intensity until in about 24 hours death supervenes; death is often preceded by clonic spasms. The virus taken from the abdominal cavity may be transmitted from animal to animal, always setting up the same symptoms. Injected subdurally the results were not so constant either as regards the production of paralysis or the transference of the disease.

Dogs inoculated, whether subdurally or subcutaneously, in seven to eight days fell into emaciation, foamed at the mouth, and became snappy; paralysis in the limbs ensued, and the animals died in 48 hours. The disease could be transmitted from dog to dog, but not to guinea-pigs. The organism described appears to assume an intermediate position between a saccharomyces and an oïdium. It is certainly pathogenetic in animals, its incubation period is comparatively prolonged, and it gives rise to paralytic symptoms; but whether it be the immediate cause of which we are in search is still doubtful, especially when regarded in the light of Dr. A. Bruschettini's experiments. This observer, using new culture media—agar or bouillon containing lecithin, cerebrin, and other substances normally present in the nervous system, and defibrinated dog's blood—was able, by inoculating with small fragments of the nervous system of a rabbit that had died after injection with "virus fixe," to obtain in from 24 to 36 hours a group of small transparent drop-like confluent colonies very slightly elevated above the surface of the special medium. These minute droplets, at first seen only with the microscope, after a time became larger, but did not grow to any very great size until the culture had passed through one or two generations on the surface of fresh media. The organism of which these colonies are made up is described as a very small, short, and thick bacillus, which stains well with Loeffler's blue and Ziehl's fuchsin. The clear band in the centre of each bacillus gives this organism a resemblance to Fränkel's diplococcus. When examined under the microscope, and when grown in fluid media, these organisms are found in regular masses of different sizes, and are arranged somewhat like the groups of diphtheria bacilli. In fluid media forms almost like cocci, and a number of small globular corpuscles, are also found. After a time the form first mentioned gradually disappears, and an organism very like the segmented diphtheria bacillus takes its place; but when fresh cultures are made, the organism again assumes the diplococcal form. It retains its vitality for at least two months at the room temperature; but in the incubating chamber it dies off in about 10 days on the solid media, and in 35 days in liquid cultures. In a vacuum it grows very sparingly; it is non-motile, and gives rise to no gas, nor to any smell; it will not grow in any of the ordinary media. Subdural injections of the third to the fifth generations killed rabbits in from five to eight days, setting up a condition indistinguishable from paralytic rabies. An emulsion of the brain and cord of animals so killed, injected into other rabbits, set up a similar condition. An organism similar to that found by cultivation was found in the nerve-centres of animals that had died of rabies and also of animals that had died after injection with cultures. Dr. Bruschettini maintains that he has isolated an organism which by its biological characters may be distinguished from all other micro-organisms; that it constantly sets up the classical form of experimental rabies; that it is possible to find it in the nervous system of rabid animals, and that he considers himself justified in regarding this microbe as a specific cause of rabies.

On the other hand, so general has been the failure to trace this hypothetical organism by any of the ordinary methods used in bacteriology, that it has been suggested that the causal organism may belong to the animal kingdom, and may ultimately be found to resemble the minute animal parasitic organisms that have been described in malarial and other similar diseases. It would appear, at any rate, that the conditions for the growth of this organism, whatever its nature, are best supplied in the cerebro-spinal system; for the poison is not only found more especially in these structures, but they seem also to be specially attacked.

This is demonstrated in a most striking fashion when the paths of infection are taken into consideration. Pasteur's early inoculation experiments were made with the saliva from a child which had been bitten by a mad dog, and in whom the disease was already established. He first reproduced the very early experiments to which reference has already been made, and found at once that on inoculating the saliva into a small pocket under the skin of a healthy rabbit the animal died in a couple of days. He found, moreover, that blood taken from this rabbit was quite as efficacious in killing another rabbit as was saliva; from this he concluded that along with the rabic poison was some septic organism similar to those that had complicated the investigation of other diseases. This supposition was corroborated when it was found that the blood of rabid animals, in which the disease had not been experimentally produced, was incapable of setting up rabies even when injected in considerable quantities. Pasteur, therefore, observing that so many of the symptoms of hydrophobia were evidently of nervous origin, in the first place prepared cerebro-spinal fluid, and afterwards an emulsion of the medulla oblongata or of the spinal cord in saline solution or broth; with these substances he injected animals subcutaneously—subdurally into the brain, or into the muscles and nerves of the limbs. By these means he was enabled to produce hydrophobia in dogs, rabbits, monkeys, and other animals with certainty, the severity of the disease being determined apparently by three factors: (*a*) the quantity of the rabic virus introduced; (*b*) the point of its introduction; (*c*) the strength of the virus as determined by the kind of animal which affords the cultivation ground for the growth of the hypothetical organism. The quantity of the virus is readily measured by making a series of dilutions; for this purpose Högyes used salt solution, and Bardach simply distilled water—the mode of dilution, however, is of comparatively slight importance.

It is a matter of common observation that slight wounds of the skin, of the limbs, and of the back are often followed by the disease after an extremely long period of incubation; whilst in lacerated wounds of the tips of the fingers where small nerves are numerous or where the muscles and nerve-trunks are reached, or in lacerated wounds of the face where there is a similar abundance of nerves, the period of incubation is usually much shorter and the disease generally much more severe. When the material from the rabic nerve-centre of a dog, or of a human being who dies of rabies, is injected into the anterior chamber of the eye, or into the dura mater of the brain, the animal so inoculated passes through a severe attack of rabies, and dies in from twelve to fifteen days. The disease may be induced with certainty when the rabic material is injected directly into a mass of muscle; or, as has already been stated, into a peripheral nerve—a method of inoculation that has been used by Tizzoni and Centanni with very great success. It will thus be seen that the two sets of conditions, natural—or rather traumatic—and experimental, run in parallel groups, the severity of the disease being usually determined by the ease with which the poison can make its way to the central nervous system. It has been assumed, indeed, by the Italian observers that, as the lymph channels of the nerves are more directly in communication with the lymph spaces in the cerebro-spinal canal than are other lymph channels, any poison introduced directly into them soon finds itself carried into positions where the conditions are favourable for multiplication and action on the nerve-centres; and is thus enabled to determine a severe attack of the disease at an earlier period than when the poison is introduced elsewhere, unless indeed it be injected directly into the cerebro-spinal system. It must be borne in mind, however, that absorption of the rabic poison may take place even from a healthy mucous surface; and the conjunctiva and the nasal mucous membrane have both been noted as unabraded surfaces from which such absorption has taken place. It is stated also that the rabic poison may be transmitted from the mother to the fœtus during intra-uterine life; and several experiments are recorded in which this has actually been brought about: though it appears to be quite possible that in such a case the absorption of a toxin may readily take place through the placenta without any actual transmission of the organisms which produce the poison. Babes, however, quite recently has denied its presence in the brain of the fœtus in utero. It has been found that the filtrate taken from an emulsion passed through a porcelain filter, when injected into a dog, may produce distinct paralytic phenomena. In consequence of this observation rabies has been defined as a toxoneurosis.

A point of very great importance in this connection is that, if the spinal cord of a dog be cut across before an inoculation of the rabic poison is made into one of the nerves of the hind foot, it will be found that if, after the disease has had time to manifest itself, two portions of the cord be taken, one below and the other above the point of section, only the emulsion made of that portion of the cord which was below will, when used for inoculation, set up rabic symptoms. The same holds good when a similar experiment is made by injecting the nerve of a fore limb. It is interesting, too, to notice that when the disease is developed slowly as the result of a bite of a limb on one side of the body, the peripheral nerves on the opposite side may also contain the rabic virus; and if used as material with which to inoculate another animal may set up a more or less virulent form of the disease. It must, then, be concluded that in order to determine the severity of the case it is necessary first to answer these two questions: (i.) Was it possible for the poison, say, from the teeth of a rabid animal, to make its way into the wound? and (ii.) Could this poison make its way to the nerve? In many cases the rabic virus may be cleaned from the teeth by the clothing which covers the bitten part; hence it is that patients bitten by animals undoubtedly rabid often escape the disease, as the leather, cloth, or other clothing material cleaned the teeth before they came in contact with the skin. It has been pointed out by Pasteur in Paris, and by Horsley in this country, that rabbits, when etherised and then presented to a mad dog to be bitten on the fur, escape the disease in a very large proportion of cases, although the teeth may have passed well through the skin: if, on the other hand, the part presented to the rabid dog be shaved before it is bitten, the bitten animals contract rabies in a much larger proportion of cases. From what has already been said, it is also evident that, where the skin is thick and the nerves few, a small quantity of virus may find its way into a wound, but does not penetrate into the nerves, and the patient may suffer no evil effects beyond those due to the bite itself. Thus is explained the fact that only about 16 per cent of the cases bitten by rabid animals appear to contract hydrophobia.

The old treatment consisted simply in encouraging bleeding from the wound; or first excising the wound and then encouraging the bleeding by means of a ligature, or by warm bathing or cupping-glasses; the raw surface was then freely cauterised with caustic potash, nitric acid, nitrate of mercury, lunar caustic, or the actual cautery. In some cases it was even recommended that the wound should be carefully sucked by a person who, of course, should have no wound or abrasion of the lips or mouth, care being taken to wash the mouth out most carefully between each application of the lips to the wound. It is doubtful whether the disease ever manifests itself after such treatment, when followed immediately by the application of a powerful caustic, and especially if the wound be small. The sufferings of the patients may be relieved by subcutaneous injections of morphia, inhalation of chloroform, or suppositories of morphia. Bromide of potassium, chloral, and Calabar bean are also recommended; three cases of cure are reported as due to curara, a drug which is tolerated in large doses in this condition. Gowers recommends doses of $\frac{1}{16}$ to $\frac{1}{2}$ grain to be given every quarter or half hour, until muscular paralysis comes on; this being repeated as the effect wears off. The same author mentions that Polli gave three grains of curara in five and a half hours to a child of twelve years of age. The patient should be placed in a quiet, warm, dimly-lighted room, and carefully watched, the greatest care being taken to prevent inoculation of wounds with his saliva; and should the nurse be bitten by the patient, as sometimes happens, especially during the hysterical and maniacal stages of the disease, the bite should be treated as that of a mad dog. Turkish, Russian, and steam baths (Buisson), and wet packs were also at one time extensively used, but with little or no good result. Tracheotomy has also been recommended where the laryngeal muscles are greatly affected; but as the respiratory muscles soon become paralysed, obviously this measure can give but temporary relief. All general treatment, indeed, is merely palliative, and is usually directed only to keep up the strength of the patient. Even Pasteur's antirabic treatment appears in most cases to be unavailing when symptoms of the disease have manifested themselves; but if this treatment can be applied during the early part of the period of incubation up to the sixth day, and, in some cases, even up to the tenth day after infliction of the wound, a much larger percentage of the cases bitten may end in recovery.

Pasteur's treatment of hydrophobia is based on the fact that rabic virus may be intensified or attenuated at will. He first observed that the tissues and fluids taken from rabid animals varied considerably in their virulence. Then followed the demonstration of the fact that the virus taken from similar positions—say the cerebro-spinal fluid—had always the same action in the same species; but that fluid taken from an animal of a different species was weaker or stronger as the case might be. Thus the cerebro-spinal fluid of a series of dogs is of constant strength, and inoculations made from dog to dog regularly produce death from rabies, the animals passing through an incubation period fairly constant in length, and through a series of similar symptoms up to death at the same term. If, however, a series of monkeys be inoculated, the virus gradually becomes attenuated; and this attenuation becomes more and more marked in successive inoculations until eventually, after the disease has run a longer and longer course in the successive animals, there comes a time at which the virus is no longer sufficiently active to cause death. If this attenuated fluid be now passed through a series of rabbits, dogs, or guinea-pigs, it comes back to such a strength that it will kill, though slowly; then, however, its virulence gradually increases until the original intensity is reached. If successive inoculations be made into rabbits with fluid either from the dog or the monkey, the virulence may be so exalted beyond that of the virus taken from a street dog, in which the incubation period is from twelve to fourteen days, that at the end of the hundredth passage the incubation period may be reduced to about seven days, or even to six. This, the strongest virus obtainable, was called by Pasteur the "virus fixe." It is even stronger than that which is obtained from rabid wolves, which at one time was supposed to be the most intense that could be obtained. Rabic virus appears also to become attenuated under certain conditions of temperature; and if it be subjected for about an hour to a temperature of 50° C. its activity is completely destroyed, or in half an hour if to a temperature of 60°. A five per cent solution of carbolic acid, acting for the same period, seems to exert a similar effect; as do likewise 1 per 1000 solutions of bichloride of mercury, acetic acid, or permanganate of potash. According to Babes, the virus rapidly loses its strength by exposure to air especially in sunlight; when protected from light and air it retains its virulence for a long period. Active virus has been obtained forty-four days after death; and it has also been obtained from a glycerine extract that had been kept for a month. It is of importance to remember this action of heat and of antiseptic and chemical substances when considering the nature of the virus; for, although permanganate of potash might act simply as an active oxidising agent upon the manufactured toxin, heat and the other chemicals appear to act rather as they are wont to do upon micro-organisms and enzymes. If so, we have additional evidence in favour of the organised nature of the virus.

Pasteur observed early in his experiments that the cords of rabbits that had been dead for some time contained less virulent poison than the cords of animals freshly killed; this was especially the case when the air was dry and the cord protected from putrefactive processes. At the end of fourteen or fifteen days the cord of a rabbit under these conditions completely loses its power of setting up rabic symptoms; in this case the time at which the virus becomes inactive appears to be determined, first, by the dryness of the atmosphere; and, secondly, by the size of the cord; as the more slender the cord the more rapid the loss of virulence. It is possible, however, that this loss of virulence may be due to a diminution in the quantity of virus rather than to any alteration in its quality, though this has not yet been proved; on the other hand, Högyes and Bardach's experiments on the dilution of the virus with saline solution, or with distilled water, appear to indicate that some such ratio of quantity to period of incubation and intensity of attack may be maintained. Italian observers, too, working on this principle, appear to have obtained satisfactory results. The most recent method of attenuating the virus is that given by Tizzoni and Centanni, who maintain that, by subjecting "virus fixe" to a process of peptic digestion by means of the addition of diluted gastric juice for varying periods, they are able to obtain rabic virus of varying degrees of intensity. This method of attenuation and intensification has been most carefully worked out; as it was evident that a method of protective inoculation must depend entirely upon the possibility of the production of protective vaccines of different strengths. In his earlier experiments Pasteur selected a series of rabic poisons beginning with that obtained from the spinal cord of the monkey—from the very weak to the strongest that he could obtain in this animal; then passing through a similar series obtained during the process of exaltation of the virus by passage through the rabbit. By inoculating dogs subcutaneously with virus taken from a series commencing with the weakest taken from a monkey, and gradually working up to that obtained from the rabbit—from the earliest to the latest in the series—the animals become immune, not only against subcutaneous injection, but against subdural injection with "virus fixe"; and also against the bite of rabid dogs.

Such a method as this, however, had several disadvantages, and was not absolutely certain in its action, as only fifteen out of twenty dogs were completely protected. Pasteur, therefore, assisted by Chamberland and Roux, devised a more trustworthy and accurate method, in which he utilised the fact that the cord of a rabic animal loses its virulence in fourteen days. A series of cords cut into short segments, which were held in series by the dura mater, were suspended in sterile glass flasks plugged with cotton-wool, and containing a quantity of some hygroscopic material such as potassium hydrate; and the whole was kept at a temperature of 72° F. (about 22° C.) The cord when taken out at the end of the first twenty-four hours was found to be almost as active as the fresh untreated cord; that removed at the end of forty-eight hours was slightly less active than that removed twenty-four hours previously; and the diminution in virulence, though gradual, progressed regularly and surely until, as already noted, at the end of the fourteenth or fifteenth day the virus was inactive. An emulsion of the cord of the last day was made, and a certain quantity injected into a dog that had been bitten; this was followed by an injection of an emulsion of a thirteenth-day cord, and so on until the animal had been injected with a perfectly fresh and therefore extremely active cord corresponding to the "virus fixe." Animals treated in this way were now found to be absolutely protected, even against subdural inoculation with considerable quantities of "virus fixe"; and thus protective inoculation against rabies became an accomplished fact.

As it would be impossible, however, or very undesirable to inject any but those persons who had actually been bitten by a rabid or presumably rabid animal, Pasteur continued his experiments in order to see whether it would not be possible to cure a patient already bitten, and, as it were, to steal a march on the virus introduced through a bite. He carried on therefore a series of experiments which led to the discovery that if the process of inoculation be begun within five days of the bite, almost every animal bitten can be saved; and that even if the treatment be commenced at a longer interval after the bite a certain proportion of recoveries can be obtained. Thus the application of this method of treatment to the human subject was not tried until it had been proved in animals that such protection could be obtained, and that such protection would last for at least two years, and probably longer. The description of the case of Joseph Meister has now become classical. This lad, nine years old, who was the first patient treated by this method, was bitten severely on the arms and legs by a mad dog on the 4th July 1885; his worst wounds were cauterised with carbolic acid about twelve hours after the bite. The dog was undoubtedly mad, and there was little chance of the survival of the patient; it was resolved, therefore, to apply to him the treatment which had been so successful in the case of dogs, and so to give him the only apparent chance of recovery. Thirteen injections were made in ten days: two on the first day with emulsions made from cords that had been exposed to dry air for fourteen and ten days respectively; two on the second day with emulsions of cords that had been exposed for eleven and eight days respectively, and then, on each of the following days up to the tenth, with emulsions of cords exposed for eight, seven, and six days down to one day; and on the last day with that of the fresh cord of a rabbit in which the virus retained its full virulence. In order to control the results, for every injection that was made into the child a corresponding one was made into a rabbit; and it was found that of the five rabbits so inoculated with the first five injecting materials not one manifested symptoms of hydrophobia; but the other eight all succumbed to the disease, the period at which they died being shorter as the cords exposed to the dry air for shorter and shorter times were successively injected. The patient, thus gradually prepared by the earlier inoculations, was not in the slightest degree affected by the stronger virus; and five years afterwards the boy was still perfectly well.

The chance of success in the human subject appears to be even greater than in the dog or rabbit, seeing that on account of the resistance offered by the human tissues to the virus, the period of incubation is comparatively prolonged; thus there is an opportunity of obtaining immunity by beginning the process of vaccination soon after the bite has been inflicted, the protection becoming complete before the incubation period has passed. Thus the virus in the system has no more chance of affecting the nerve-centres than has the "virus fixe" when injected under the dura mater; the nerve-centres having become gradually acclimatised, as it were, to the presence of the rabic virus, and able to carry on their proper functions even in its presence; until in time, like the microbial poisons, it is gradually neutralised and eliminated from the body. In his earlier experiments Pasteur injected emulsions made from the cords until the five days' cord was reached; but after a time he used injections of cords up to the third day. This "simple" method, as quoted by Roux, is given in the following table:—

Day of Treatment.	Number of Days that Brain had been desiccated.	Dose injected.
1st day,	Brain of 14 days,	In dose of 3 c.c. of emulsion.
	13 ,,	,, ,, ,,
2nd ,,	,, 12 ,,	,, ,, ,,
	11 ,,	,, ,, ,,
3rd ,,	,, 10 ,,	,, ,, ,,
	9 ,,	,, ,, ,,
4th ,,	,, 7 ,,	,, ,, ,,
5th ,,	,, 6 ,,	,, 2 c.c. ,,
	6 ,,	,, ,, ,,
6th ,,	,, 5 ,,	,, ,, ,,
7th ,,	,, 5 ,,	,, ,, ,,
8th ,,	,, 4 ,,	,, ,, ,,
9th ,,	,, 3 ,,	,, 1 c.c. ,,
10th ,,	,, 5 ,,	,, 2 c.c. ,,
11th ,,	,, 5 ,,	,, ,, ,,
12th ,,	,, 4 ,,	,, ,, ,,
13th ,,	,, 4 ,,	,, ,, ,,
14th ,,	,, 3 ,,	,, ,, ,,
15th ,,	,, 3 ,,	,, ,, ,,

It was soon evident, however, that, although this method was efficacious where the wounds were not severe, and were confined to parts in which the nerve-supply was not extensively interfered with, it was often quite inadequate in serious cases, as of wounds about the face, or of wounds inflicted by a mad wolf, the virus of which is more active than that of the rabid dog of the streets. In these latter cases the number of injections which, in the simple treatment, are spread over five days, are made in three days; then, on the fourteenth day, a fresh series of injections, or rather repetitions, is begun, which lasts until the twenty-first day. This "intensive" method is given in the following table:—

Day of Treatment.	Number of Days that Cord had been desiccated.	Dose injected.	Day of Treatment.	Number of Days that Cord had been desiccated.	Dose injected.
1st day, morn.	14 days	3 c.c.	8th day	4 days	2 c.c.
	13 ,,		9th ,,	3 ,,	1½ c.c.
even.	12 ,,		10th ,,	5 ,,	2 c.c.
	11 ,,		11th ,,	5 ,,	2 c.c.
2nd ,, morn.	10 ,,	3 c.c.	12th ,,	4 ,,	2 c.c.
	9 ,,		13th ,,	4 ,,	2 c.c.
even.	8 ,,		14th ,,	3 ,,	2 c.c.
	7 ,,		15th ,,	3 ,,	2 c.c.
3rd ,, morn.	6 ,,	2 c.c.	16th ,,	5 ,,	2 c.c.
even.	6 ,,		17th ,,	4 ,,	2 c.c.
4th ,,	5 ,,	2 c.c.	18th ,,	3 ,,	2 c.c.
5th ,,	5 ,,	2 c.c.	19th ,,	5 ,,	2 c.c.
6th ,,	4 ,,	2 c.c.	20th ,,	4 ,,	2 c.c.
7th ,,	3 ,,	1 c.c.	21st ,,	3 ,,	2 c.c.

Babes, in order to obtain a constant virus, makes a mixture of cords which have been exposed to the drying process for three or four different periods. He inoculates at least twice a day, and in very severe cases more frequently; moreover, he uses larger quantities of the protective material and continues the treatment over a longer period of time. Babes has recorded a most convincing example of the success of this treatment, and of the importance of the factor of time between the bite and the commencement of the treatment. Thirteen men and thirty animals—cattle, horses, pigs, and dogs—were attacked by rabid wolves. Of the thirteen men so attacked twelve came under treatment; all recovered except one, whose head and face were frightfully torn and lacerated: the thirteenth man, who did not present himself for treatment, died of hydrophobia; and every one of the thirty animals attacked succumbed to typical rabies. The treated patient who died succumbed ten days after the completion of a very intense and prolonged treatment (thirty-two days). After his death the other patients were subjected to a further six days' treatment with emulsions made from two cords each of a whole series, beginning with those exposed for twelve days and passing up to those exposed for one day. No other patient died. It is now generally acknowledged that, when the operation is properly performed, the injection even of very large quantities of virus may be safely carried out; and, as we have seen that in the intensive method, where these large quantities are injected, greater success is obtained, there seems to be a possibility that the mortality may be still further diminished even by Pasteur's method of treatment.

STATISTICS of CASES treated in the Pasteur Institute, Paris, not including persons in whom the disease declared itself during course of treatment, in which therefore the treatment was not complete.

A. *Cases excluded in which the disease declared itself within a fortnight after inoculation.*

Years.	Persons Treated.	Deaths.	Mortality per cent.
1886	2671	25	0·94
1887	1770	14	0·79
1888	1622	9	0·55
1889	1830	7	0·38
1890	1540	5	0·32
1891	1559	4	0·25
1892	1790	4	0·22
1893	1648	6	0·36
1894	1387	7	0·50
1895	1520	2	0·13

B. *All cases included in which treatment was completed.*

Years.	Persons Treated.	Deaths.	Mortality per cent.
1886	2682	36	1·34
1887	1778	21	1·18
1888	1625	12	0·74
1889	1834	10	0·54
1890	1546	11	0·71
1891	1564 + 5[1]	9	0·57
1892	1793 + 5[1]	7	0·39
1893	1648 + 4[1]	6	0·39
1894	1392	12	0·86
1895	1523 + 1[1]	5	0·33

In 1895 Lebell and Vesesco record the recovery of a patient in whom hydrophobia had declared itself during the course of treatment. The case was that of a child six years old brought to the Antirabic Institute at Jassy in August 1894 after being bitten in various places on the face, arms and hands by an undoubtedly mad dog. Symptoms of rabies of a severe character interrupted the treatment, but it was resumed on their abatement. The child received altogether, besides the cords of Pasteur's series, 87 grammes of an emulsion of "virus fixe" heated at 80° C.; it ultimately got well and was in good health at time of record. The clinical symptoms were all diagnostic of hydrophobia.

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[1] These cases are not included in the calculations as the patients died from the results of the bite during the course of treatment.

As early as 1889 Babes and Lepp had conceived the idea that it might be possible by means of the blood to transmit conferred immunity from rabies from one animal to another. Although the success of these investigators was not great, Tizzoni and Schwarz, and later Tizzoni and Centanni, worked out a method of serum-healing and protection in hydrophobia which is worthy of attention. In this method not the rabic poison itself, but the protective material formed is injected into the tissues. These observers showed that the serum of vaccinated animals is capable of destroying the pathogenetic power of the virus of rabies—"virus fixe"—not only when mixed with it before injection, but even when injected simultaneously, or within twenty-four hours after the introduction of the virus into the body. They showed also that the serum of a rabbit protects a rabbit better than does the serum of a dog; and they indicated that by their method they were able to obtain a higher degree of immunity than could be obtained by Pasteur's method. Taking "virus fixe" as their starting-point they prepared a series of weaker materials by submitting it to the action of gastric juice; beginning with a weak virus so prepared and using a series gradually becoming stronger, they protected not only rabbits and dogs but sheep also against the most virulent rabic poison, even when introduced under the dura mater. By continuing the process they succeeded in twenty days, after seventeen injections, in obtaining such a large quantity of the antirabic substance in the serum that, if injected twenty-four hours before the poison, even so small a proportion as 1 to 25,000 of serum to body weight would protect the animal. More powerful serum still is obtained when the sheep are revaccinated; the injections in this case are made during the course of twelve days, each injection again consisting of 0·25 gramme of the emulsified cord per kilogramme of the weight of the sheep. This process may be repeated again and again so long as the intervals are sufficient to allow the animal to keep in good condition; of this the best criterion is the maintenance or increase of its weight during the process of vaccination. The series of vaccinations may be repeated at intervals varying from two to five months. In such cases the protective power of the serum against rabies is maintained at a level sufficiently high and constant to neutralise the effect of a lethal dose of rabic virus when injected under the dura mater: these experiments were carried out on rabbits. The vaccination is usually made into the subcutaneous connective tissues of the sheep; and it appears, as a result of the process of immunisation that follows, or perhaps runs concurrently with it, that an antirabic substance is produced in the blood which, if introduced into the unprotected animal along with the rabic virus, exerts a special protective or curative action upon it. It seems, according to the observations of the authors, that the best time after the completion of the vaccination process at which to take the blood and separate the serum which contains the antirabic substance is probably about the twenty-fifth day after the last of the injections of rabic material into the animal immunised for the production of the antirabic serum. It was only with serum taken at such time that the calculated dose proved perfectly efficacious on all the animals subjected to experimental tests. From this important observation we gather that the rabic virus, whatever its nature, may remain in the blood for this length of time unchanged or unneutralised. During the course of such diseases as diphtheria and tetanus the poisonous albumoses appear to be stored up in the spleen, and perhaps also in other organs, for a considerable length of time before their excretion; and it is quite possible and even probable that some such storage and gradual passage into the blood may occur also in the case of rabies. If this be the case, it is evident that part of the antirabic serum may be used up in neutralising the unaltered rabic poison. The second point to be observed is that, for at least the period above named, the antirabic substance must remain in a comparatively stable condition, or gradually increase in strength; and experiments go to prove that it may be maintained at the same level of activity even for a longer period.

This method of treatment has thus been brought well into line with that of the other specific infective diseases in which serum-therapy has been developed; and there can be little doubt that if this method be as successful as the process of rapid immunisation of the patient worked out by Pasteur, it has many marked advantages and apparently few disadvantages. Not the least of the advantages is the very important one that, if the serum be evaporated down to dryness and protected from air and light, it will remain unchanged for a considerable length of time without putrefaction, and without loss of its antirabic virtue. In this form the substance may be easily transmitted by post; it dissolves rapidly in distilled water or sterilised normal saline solution, and the dosage is very easily managed. Many of the difficulties associated with the Pasteur system are thus entirely done away with; the patient need not leave his home, and the method of exhibiting the serum is so simplified, that it is merely necessary to take precautions to prevent the access of extraneous organisms along with the injected material. Such a serum may be kept in stock, and is ready at any time to be applied to the treatment of a patient bitten by a mad dog; and the patient may at once receive that quantity of the antirabic serum, or of the antirabic substance contained in the serum, which, under the Pasteur method, could only be manufactured in the body of the patient himself after a somewhat prolonged process of vaccination, with series of virus gradually increasing in strength. This is a most important feature, as, reasoning from analogy, the earlier the poison can be neutralised the less is the amount of antitoxic substance necessary to bring the case to a successful issue. Although it would certainly be dangerous to delay the process of treatment beyond the term indicated by Pasteur as that after which there is comparatively little hope of success, it is evident that, if a sufficient amount of the antirabic substance could be directly introduced, the fatal effects of the poison might be neutralised in a certain proportion of patients who otherwise must inevitably be lost. With these advantages there are apparently no counterbalancing disadvantages, as the serum appears at worst to be quite harmless. This process in its two stages, then, differs from that developed by Pasteur, and at present in use, in so far that, in place of promoting the formation of the antidote within the body of the patient by a process of vaccination with progressively stronger and stronger virus, Tizzoni and Centanni in Italy, and Babes in Bucharest, do this part of the process in an animal; Babes using the dog, Tizzoni and Centanni the sheep. From animals so prepared the antirabic substance is conveyed to the patient or animal to be treated along with the blood serum in which it is dissolved, which acts merely as a vehicle.

The second modification made by the Italian observers is that, instead of using Pasteur's method of protective vaccination for the animals from which the serum is to be obtained, they use a vaccine which has been modified or attenuated by a process of peptic digestion. The exact action of this digestive process has not as yet been discovered. Some have suggested that we have to do merely with a somewhat complicated process of dilution; but, although dilution, as already pointed out, may undoubtedly play a very important part, it appears more probable that we have to do with a positive reduction in the activity of the poison-secreting organisms; or with such a diminution of the potency of the ferment produced by them, that the tissues are not prevented by their presence from reacting and performing their proper functions. Whatever may be the cause, the activity of the virus is so modified that considerable doses may be injected within a comparatively short period, even when protection has not been carried very far.

In many respects the method of obtaining the antirabic serum resembles that by which the tetanus and diphtheria antitoxic serums are obtained. As already pointed out, this serum, when mixed in definite quantity in a test-tube with a lethal dose of canine virus or "virus fixe" and then injected into a rabbit, so neutralises the poison that there is neither any increase in the quantity of the virus nor any appearance of the symptoms of rabies even in animals kept under observation for so long a period as five months. [*Vide* chapter on "Snake-Bite," p. 809.] Again if, after the administration of a lethal dose of the poison, the serum be not injected at once an alleviation is still obtained; but under this condition a somewhat larger quantity has to be injected in order to keep the animal alive. The amount required, however, increases so slowly that if the injection of serum be delayed until the end of the first half of the incubation period, it is only necessary to multiply the dose of the serum some six or eight times. In this respect the serum treatment in rabies has great advantages over the other serums now in general use. In the case of diphtheria, after the poison has once got a foothold, the dose has to be multiplied some twenty to one hundred times in order to obtain favourable results; and in the case of tetanus the dose, if withheld until the later stages of the incubation period, must be increased to from one to two thousand times.

Antirabic serum exerts a distinct prophylactic effect, and it appears by experiment that, when injected in small doses even a comparatively short time before the patient is bitten, protection against an attack of rabies is obtained. Such prophylaxis, of course, could only be needed by those who are frequently in contact with dogs; or by persons working for any length of time with rabic virus, to whom some such protective inoculation would be of enormous value. It will be remembered that, as in the case of tetanus, the rabic poison has a very definite selective action; it seems to pick out the nerves and the central nervous system for its attack. We find, accordingly, that by selecting the site for the injection of the serum much better results may be obtained, even with the use of smaller doses. It is found, for instance, if the serum be injected under the dura mater of the brain that much smaller doses are needed than when the injections are made into the substance of a nerve; and that for subcutaneous injection of the serum a larger dose is necessary than when it is injected into either of the above positions. The serum, when injected into the nervous tissues, may act at once, possibly by a direct chemical antagonism to the virus; though very little evidence from direct experiment can be brought forward in favour of this supposition. On the other hand, it is maintained by some investigators that the serum in the nerve-centres probably acts not upon the nerve-cells only, but also upon the cells of the neuroglia, which with its aid, perhaps through some special stimulation, are able to carry on their functions in the presence even of considerable quantities of the rabic virus. It appears to be in some such way as this that the point of introduction of the protective serum determines the ultimate result of the inoculation; when the serum is injected subcutaneously it is possible that a large proportion of its active material is used up and practically wasted in fortifying or assisting cells which stand in less need of protection; whilst the nerve-cells, participating only in the general distribution of the antirabic substance, do not receive from it sufficient help to enable them to withstand the action of the poison which, as we have seen, appears to be especially mischievous to them. When, on the other hand, the serum is injected into the substance of a large nerve, the protective agent finds its way at once into channels which communicate almost directly with the cerebro-rachidian lymph system; and thus larger quantities of it come into direct contact with the cells or tissues of the central nervous system. In the case of a subdural injection of the serum the antitoxic material comes primarily and directly into contact with those tissues which stand most in need of its protective action; consequently the best results are obtained.

One great difficulty about the production of serum for this method of treatment is that, up to the present, it has been found impossible to grow the rabic virus outside the body of an animal; the vaccine material can therefore be obtained only in comparatively small quantities and with the expenditure of a great amount of time, trouble and money. Moreover, the virus is obtained in such a form that it is difficult, if not impossible, to separate the whole of the active portion of the poison from its ordinary vehicle; whilst, as we are still in ignorance of the exact form of the poison-producing organism, we are not in a position either to isolate the latter, or to separate an active vaccinating material by precipitation, filtration, or the use of chemical or microbicidal agents. The serum treatment is still in its infancy, and it is quite possible that in certain cases it may not prove so efficacious in general practice as it has been found to be in experimental work; but, from an experimental point of view, the results are so striking that we may hope for results as good or almost as good in the treatment of hydrophobia in man. It has been alleged that in certain cases excision of the wound before the appearance of symptoms of hydrophobia has been attended with success, especially if the whole cicatricial tissue and the surrounding parts have been freely removed. No doubt some such treatment might be successful if carried out at a very early moment; but it seems to be very doubtful whether, on the whole, such treatment could be of more value than the application of powerful caustics. Our statistics under this head are too few to carry us beyond conjecture.

GERMAN SIMS WOODHEAD.

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G. S. W.

GLANDULAR FEVER

(Drüsenfieber)

Glandular Fever may be defined, provisionally, as an acute infectious fever, characterised by inflammatory swelling of the deep cervical and other lymphatic glands, and by constipation; and followed by a considerable degree of anæmia and depression.

Pathology.—E. Pfeiffer described the disease in 1889, and expressed the opinion that it was an acute specific fever previously unrecognised. He pointed out that it occurred in narrowly limited epidemics, but that most of the children of a family in which one member suffered contracted the disease. This observation has been confirmed by later writers; and Park West states that, in an epidemic affecting an isolated community in Ohio, ninety-six cases occurred among the children of forty-three families; only about twenty children between the ages of seven months and thirteen years escaped. From the occasional occurrence of nephritis as a complication, Hesse has drawn an argument in favour of the contention that the disease is specific, as Pfeiffer maintained. The onset of the disease is acute, and the adenitis one of the earliest symptoms; while pharyngitis, though it may occur as a complication, is seldom severe. Park West observed only four cases of severe pharyngitis in ninety-six cases; and usually there is no pharyngitis at all. That the disease is not an aberrant form of mumps is shown by the fact that parotitis has not been known to occur; and that in the Ohio epidemic it was ascertained that fifty-seven of the ninety-six children had had mumps before the glandular fever, or soon after it. The suggestion that the cases are examples of rubella, or some other exanthematous fever without the exanthem, is not tenable in view of the fact that intermediate cases with rash have never been observed, and that in the extensive Ohio epidemic no rash was observed in any of the cases. The adenitis runs a fairly regular course, reaching its maximum in from two to four days, and then subsiding gradually, while at the same time groups of glands other than those first affected may be enlarging. The glands show little tendency to suppurate; indeed it is very doubtful whether this accident ever happens.[1] Bacteriology has not as yet thrown any light on the pathology of the disease, but no thorough examination has been made. The obstinate constipation characteristic of it, coupled with the frequency of enlargement of the mesenteric glands, led v. Starck to suggest that the general symptoms and the adenitis were due to infection derived from the intestines, or were produced by the absorption of toxins from the retained fæces. The place of the disease in nosology would appear to be near bubonic plague, to the milder forms of which (*pestis minor*) it bears some resemblance [*vide* vol. i. p. 928].

Course.—The incubation period is probably about seven days, with extremes of five and ten days. The onset is sudden; complaint is made of pain in the neck, which is held stiffly, of pain on swallowing, and sometimes of pain in the abdomen. The face is flushed, there is tenderness in the anterior triangle, the temperature is 101°-103° F., the tongue is furred, there is anorexia, sometimes vomiting, rapid pulse, and the ordinary symptoms of pyrexia. Examination of the throat reveals no condition sufficient to account for the stiffness of the neck and dysphagia, nor for the pyrexia. The mucous membrane may be healthy, or a little reddened; or there may, of course, be chronic granular pharyngitis or tonsillitis, which affections are extremely common in children. On the second or third day of fever an elongated swelling, uniform to the eye but on palpation found to be due to three or four enlarged glands, is perceived beneath and towards the front of the sterno-mastoid muscle. In nearly all cases the adenitis is first perceptible on the left side; it reaches its maximum in from two to four days, and then begins to subside. A little before the swelling on the left side reaches its height the corresponding glands on the right side begin to swell, and they run through a similar course. Other groups of glands, the posterior cervical, the axillary, the inguinal, may likewise become enlarged and tender. Abdominal pain and tenderness and enlargement of the liver are present in most cases; enlargement of the spleen and of the mesenteric glands occurs in many, probably in more than half. Constipation is obstinate except in the very mildest cases, in which it may be replaced by frequent small mucous stools. In some severe cases the beginning of convalescence is marked by the passage of a large amount of green mucoid material from the bowel. The temperature usually attains its maximum (104° F.) about the third day, and remains high so long as groups of glands continue to enlarge. The pulse may continue rapid for a day or two after defervescence, which takes place usually during the second week. Complications are rare, the most important being nephritis, which may be attended by hæmaturia; but the disease usually runs a benign course, though occasionally, as Moussous has pointed out, the general symptoms are so severe as to suggest typhoid fever. Convalescence is apt to be prolonged, the child being left in a condition of general depression with anæmia, from which complete recovery does not as a rule take place in less than a couple of months. The enlarged glands subside gradually, and have disappeared before the general health is completely restored.

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[1] Comby's opinion to the contrary appears to rest on Neumann's observation of the presence of staphylococci in certain cases; but Neumann himself held that the cases he was dealing with were not examples of Pfeiffer's Drüsenfieber.

Age.—The disease is one which affects children; it is not uncommon in infancy, but must be very rare after puberty; though Donkin and Coutts have recently mentioned instances in which young adults were affected during a family epidemic.

Treatment has little or no effect on the course of the disease. The pain in the neck and swollen glands may be relieved by a cold compress, or by belladonna fomentations, but these measures do not prevent the development of adenitis on the opposite side. Constipation can be relieved by a full dose of calomel; but the condition returns at once, and Park West saw reason to believe that this treatment was followed by greater depression and a more prolonged convalescence. Small doses of calomel (gr. $\frac{1}{10}$ to $\frac{1}{12}$) are probably of use in regulating the bowels and preventing decomposition in the intestinal canal. During the fever the child should be kept in bed or on the couch, and should have simple liquid nourishment. During convalescence it should be guarded from over-fatigue or exposure to cold, and should receive as much nourishing food as it can digest. Cod liver oil and iron preparations, or the syrup of the phosphate of iron, are indicated; and as soon as the enlargement of the glands has disappeared change of air may be advised.

DAWSON WILLIAMS.

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D. W.

DISEASES DUE TO PROTOZOA

42. MALARIAL FEVER.
43. HÆMOGLOBINURIC FEVER.
44. AMŒBIC DYSENTERY.

MALARIAL FEVER

(PALUDISM)

Definition.—A specific, infectious disease, caused by the hæmatozoa of Laveran, and characterised clinically by very variable types of fever—some regularly intermittent, others remittent or continuous—variations which appear to depend upon differences in the form and mode of growth of the infecting organisms.

Historical note.—From the voluminous, one may say chaotic, literature of malaria, the following features may be selected for special mention:—

The writings of the Greek and Roman authors, from Hippocrates to Celsus, show a remarkable knowledge of the clinical features of the disease. They even recognised the mild character of the spring in contrast to the more pernicious type of the autumnal malarial fevers.

The writings of Richard Morton, in whose *Pyretologia* (1692) is recognised clearly the association of malaria with unhealthy localities and bad air.[1]

The introduction of Peruvian bark into Europe in the seventeenth century, and the powerful advocacy of it by Sydenham and by Morton.

And lastly, the discovery by Laveran, in 1880, of the parasites of the disease, which has established on a firm basis the etiology and pathology, and has given an infallible diagnostic test by which the malarial can be recognised from all other fevers.

Etiology.—Though one of the most widely spread of the specific fevers, malaria has latitudinal limits; inasmuch as it is not met with higher than 60° north in the eastern hemisphere, while in the western hemisphere it is now rarely seen above 45° north. The disease increases progressively towards the equator.

The altitudinal limits of the disease have long been recognised. As a rule it is not found in regions from 1000 to 2000 feet above the sea-level, though in India and in Persia it has been met with at elevations considerably higher. The principal foci of the disease all the world over are along the deltas and courses of the great rivers.

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[1] Although, among modern writers the credit of associating malaria with noxious and miasmatic effluvia is usually given to Lancisi, it belongs in reality to Richard Morton, whose *Pyretologia* contains the most systematic account of the disease in the seventeenth century. The paragraph is as follows, taken from the Amsterdam edition of 1696:—"Aer item externus, praesertim Palustris vel Autumnalis inspiratus, et cum spiritibus commixtus, particulis heterogeneis et venenatis ita nonnunquam refertus est, ut Febres intermittentes non aliâ de causâ in locis palustribus et oris maritimis Endemiae sint, atque Autumnali tempore ferè ubique Epidemicae evadant."—W. O.

In Europe paludism has gradually lessened, and now it is a rare affection in England, France, and Germany, though it still prevails extensively in Italy, in Greece, and in the regions of the Lower Danube. In Africa it extends from Algeria in the north to the 30th parallel south, and it proves terribly fatal to Europeans in the basins of all the large rivers. Throughout India and China and the Malay Peninsula the disease is endemic in low-lying districts and in the deltas of the great rivers. In the smaller islands of the Pacific, and in the large islands north of 25° N. and south of 20° S., malarial fevers are rare.

In North America malaria is now almost unknown above the 45th parallel. On the Atlantic sea-board above the 40th parallel it has diminished gradually; in Pennsylvania, New York, and the New England States true intermittents are rare. In the region of the river St. Lawrence the disease does not exist. Of the great lakes, the littorals of Ontario, Huron, and Superior are now almost free; while in certain regions of the shores of Lake Michigan and Lake Erie the disease still prevails. Throughout the Southern and some of the Western States malaria prevails, but appears to be diminishing in virulence. In the W. Indies, and in Central and S. America, it still holds its ground.

An interesting feature in connection with the disease is its gradual disappearance from certain regions under the influence of drainage and cultivation. In England, even in the Fen country, it is now almost unknown. In New England, too, it has gradually disappeared. In parts of Canada, bordering Lake Ontario, which were formerly hot-beds of the disease, cases only exceptionally occur.

Malaria has been well called a *soil* disease. Cruising in the most malarious regions of the tropics sailors are not attacked unless they go ashore. The physical factors of the land are of the first importance. Dry, sandy soils are, as a rule, exempt; the chief factor being a high subsoil humidity, such as is met with in marshy land in which there is stagnation of the water. Excavations of all sorts, extensive cuttings for railways, and the breaking up on a large scale of virgin soil have in many instances been followed by outbreaks of malaria. The greater prevalence of fever in the Royal Engineers in comparison with other troops is probably to be accounted for by their more frequent employment in the excavation of soil.

Next to the soil and humidity, high temperature seems to be the most important factor; and the disease increases almost in direct proportion to the height of the mean temperature of the summer months.

Suitable soil, temperature and humidity, though important, are not the only factors; since, as has long been known, various tracts in which all the surroundings appear most favourable to malaria, are entirely free from the disease. In many marshy regions the disease has disappeared completely without any accompanying change in the soil or humidity. The additional element is the specific organism of the disease, which finds in the marsh-soil, the heat, and the moisture, the conditions of its external development.

Medium of infection.—It is universally acknowledged that in the large majority of cases the air is the medium of infection; whether the disease may also be directly conveyed by water has been much disputed: general opinion in the profession favours the view, experimental evidence is directly against it. Persons have been allowed to drink water from the Pontine marshes without ill effects; and in Baccelli's clinic at Rome experiments were made in thirty cases with water from malarial districts without a single positive result. Grassi could not produce the disease with dew from malarial regions, or by allowing healthy men to drink blood from malarial patients.

The *seasonal relations* of malaria are interesting. It is a disease of the warmer months. In temperate climates, as has been recognised from the days of the Greek physicians, there have been spring and autumnal outbreaks, the latter being the more severe. In this latitude we have, as a rule, a group of spring and early summer intermittents; and then in August, September, and October the cases show greater irregularity and occasionally occur in more pernicious forms. In an analysis of 614 cases in the medical department of the Johns Hopkins Hospital by Thayer and Hewetson (1), the smallest number of cases occurred in the months of December, January and February. There was then a steady increase until the month of May, which showed the spring maximum. In July the increase began again, and the climax was reached in September, when 156, or more than a fourth of all the cases, began to have their first symptoms.

Race.—The Caucasian seems more subject to the disease than the brown or black races. Of 614 cases of malaria just referred to there were only 4 per cent of the negro race; and the attendance of coloured people at the hospital during the same time was 12·2 per cent.

Age.—While no age is spared, children and young adults are most often attacked. Of 614 cases there were 106 under twenty years of age, and 207 between twenty and thirty.

Sex.—Of 614 patients only 121 were females. The greater liability of men to infection depends upon the much greater frequency with which they are exposed in their occupations; in this latitude (Baltimore) sailors and fishermen are particularly prone to the disease.

The Parasites of malarial fever.—It is difficult to say who first propounded the doctrine of a *contagium vivum* in malarial fever. Dr. Charles, in a postscript to the translation of the work of Marchiafava and Bignami, quotes the following remarkable paragraph from Rasori, who wrote in 1846:—"For many years I have held the opinion that the intermittent fevers are produced by parasites, which renew the paroxysm by the act of their reproduction, which recurs more or less rapidly, according to the variety of the species."

One of the first systematic attempts to formulate a theory of the parasitic nature of the disease was in the work of J. K. Mitchell (2). Then followed a series of observations, necessarily crude and unscientific, in which attempts were made to prove the connection of the disease with various forms of algæ.

In 1879 Klebs and Tommasi-Crudeli announced the discovery of the *bacillus malariæ*, and for several years subsequently the work done in the various Italian laboratories seemed confirmatory. The observations of Golgi and of many others have shown, however, that this organism has nothing whatever to do with the disease.

In 1880 Laveran announced the discovery of certain parasitic bodies in the blood of patients with malarial fever. He recognised that they were parasites, and raised the question whether they were amœbæ. Subsequently, influenced no doubt by the presence of the motile filaments, he suggested the term *oscillaria malariæ*. Though of course subsequent work has enormously enlarged our knowledge of these bodies, the credit for their description, and for suggesting their relations to the disease, rests wholly with Laveran. Marchiafava and Celli described with great accuracy the intra-corpuscular amœboid form, to which they gave the name *plasmodium*.

The most important additional fact was added by Golgi, who pointed out the association of the paroxysm with the segmentation of a group of the malarial organisms. The net results of the past ten years have been the full confirmation of Laveran's work, and the differentiation by the Italian observers of varieties of the parasite in the different clinical forms of the disease.

The records of the subject have become very voluminous; and a complete bibliography (to May 1895) is given in the monograph of Thayer and Hewetson above mentioned: to this the reader is referred.

Methods of examining the blood.—The necessity of working with high powers, a twelfth immersion with a good condenser, has been a great drawback to the study of the parasites of malaria. At the same time it enhances greatly the credit of Laveran that his work was done with much lower powers.

The fresh blood should be examined; the drop may be taken either from the tip of the little or ring fingers, or from the lobe of the ear. It is important to cleanse the skin thoroughly and to wipe it dry, so as to avoid dirt and perspiration. A very small drop should be taken, and care must be exercised that the cover-slip when pressed against the blood-drop does not touch the skin. The drop should be so small that the corpuscles are spread out in a uniform layer, and are not in rolls. The intra-corpuscular form cannot be well seen unless the blood-disc presents the flattened surface. For making permanent preparations the blood is collected in the usual way upon the cover-slips, is fixed by heat or by alcohol, and then stained with methylene blue and eosin.

1. *Parasite of the simple Intermittent Fevers.*

(*a*) *Tertian Fever.*—In the blood of a patient examined within twelve hours after the chill in tertian fever, one sees inside the red blood corpuscles small, pale, hyaline amœbæ, which undergo changes in shape, often assuming the form of a star or of a cross (Fig. I. 2 and 3). There may be no pigment visible, and to these hyaline bodies Marchiafava and Celli gave the name of *plasmodia*. In a few examples one may see scattered pigment granules in the amœbæ (4), usually peripherally placed. If the examination is made at intervals of six or eight hours the hyaline bodies are seen to have grown, are more pigmented, and the corpuscles containing them have become gradually paler and somewhat expanded (5, 6, and 7). The pigment granules, which at first are very small, increase in size and display very active movements. In Fig. I. the corpuscles from 2 to 7 illustrate the form and the gradual growth of the organism within the corpuscle. At the end of forty-eight hours it occupies the entire corpuscle, which looks like a thin, translucent shell usually devoid of colour. The organism then undergoes the remarkable change known as segmentation, which precedes and is associated with the chill and fever. The pigment becomes motionless and is gradually collected towards the centres of the amœbæ (8) until it is in the form of a closely packed more or less central clump or clumps. The protoplasm becomes more finely granular, and indistinct lines of striation are seen (9), which begin at the periphery. At this stage the organism may present the appearance of a beautiful rosette, as figured at Fig. I. 9 and 10. The segmentation progresses until the entire protoplasm is divided into from twelve to eighteen or twenty spheres (10). The shell of the corpuscle containing the parasite usually bursts, and the small, rounded hyaline bodies are set free. Each one of these little bodies, as represented at Fig. I. 11, consists of a translucent protoplasm, with a central, more highly refractile spot.

The segmentation is regarded as a reproductive process, and these small spherical bodies are believed to be the spores, which penetrate a new set of corpuscles, and so begin a new cycle of development. The presence of the segmenting forms is invariably associated with the paroxysm. On finding them in the blood one can predict with certainty that a paroxysm is imminent. In quotidian fever we have to deal with two groups of tertian (or three groups of quartan) parasites maturing on successive days; and the full-grown segmenting forms of to-day's paroxysm and the half-grown organisms of to-morrow's attack are to be found in the blood.

(*b*) *Quartan Fever.*—The early forms within the red blood corpuscles are amœboid bodies similar to those of tertian fever. Soon (Fig. II. 2), however, it is noticed that the pigment is different; the granules are larger and blacker (Fig. II. 3 and 4), and the amœboid movements are not so active. In their growth the parasites do not decolorise the corpuscles, which sometimes have a greenish, very brassy look. From the sixty-fourth to the seventy-second hour the amœbæ have reached their full development, occupying the greater portion of the affected corpuscles; but a thin rim of coloured stroma can usually be seen (Fig. II. 8-10). Some of the corpuscles are completely filled by the parasites (Fig. II. 11). Even at this stage a skilled observer can usually recognise the quartan from the tertian organism. The pigment granules then collect towards the centre; and in so doing usually form distinct rays (Fig. II. 12). Then, as in the tertian form, the organism begins to segment; a marginal indentation is first seen, with lines of radiation, and a beautiful rosette is formed which segments into from six to ten, occasionally twelve, small spherical or ovoid bodies (Fig. II. 13, 14, and 15). The character of the pigment, the smaller size of the organism, the smaller number of segmenting forms, and the length of the cycle of development, are differences which separate the quartan from the tertian variety.

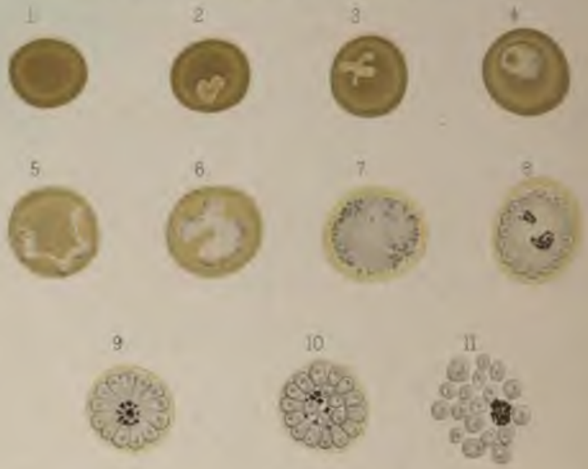
In the quartan malarial fever the blood may show two or more groups of parasites. There may be two groups which reach maturity on successive days, with one day of interval—double quartan fever; or there may be three groups of organisms maturing on successive days, causing daily paroxysms—triple quartan fever. In this latitude quartan infections are very rare.

2. *The parasite of the irregular Malarial Fever.*

In the more irregular types of malarial infection, which are met with in the autumn months, a third variety of organism may be recognised, which has been specially studied by the Italian observers. The early form of this parasite is not unlike that of the tertian and quartan varieties; but the hyaline body is more ring-like, more highly refractile, and the central part often looks shaded, as if a more solid body were enclosed within a vacuole (Fig. III. 1-6). As this form increases the amœboid movements are well seen. The pigment is in small amount, at first in the form of one or two very dark granules at the margin of the amœbæ; and the pigment never becomes so abundant as in the tertian or quartan forms. The organism rarely occupies more than about one-third of the corpuscle, the stroma of which is never entirely decolorised. On the contrary it often presents a curious brassy green appearance, and looks shrunken or crumpled (Fig. III. 7). The cycle of development of this form is rarely carried out entirely in the circulating blood, but the bodies with centrally placed pigment are not uncommon. The observations of the Italian observers seem to show conclusively that the segmentation (Fig. III. 14-16) takes place in the spleen and in the bone-marrow and internal organs. The length of its cycle of development has not been determined. Probably different groups mature at varying intervals of time. The fever associated with this organism is characterised by irregularity, the paroxysms are not at definite periods, and the pyrexia may be more or less continuous, with remissions. This form is associated with the severer types of the malaria seen in the late summer and autumn—the æstivo-autumnal fevers of the Italians.

I.

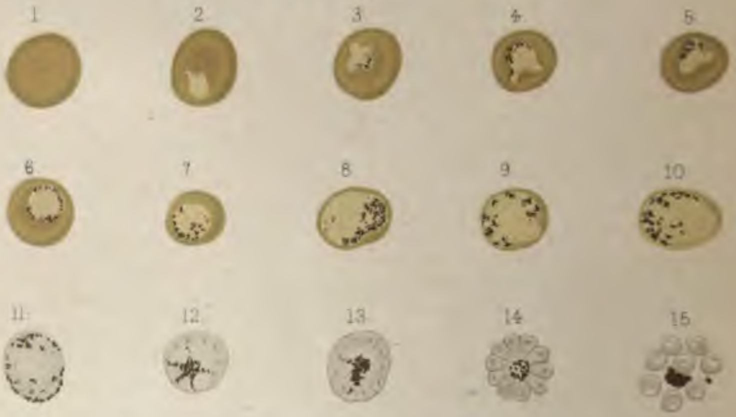
The Parasite of Tertian Fever.



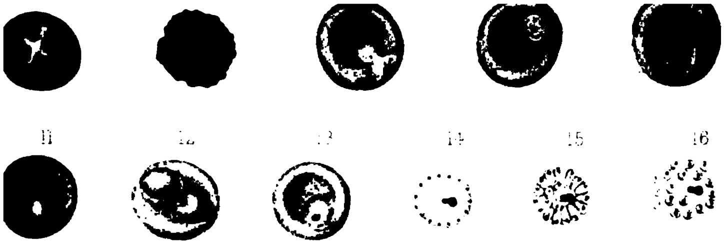
FIGS. 1–11 show the gradual development of the amœba within the red corpuscle. Figures 3–6 show the amœboid changes.

II.

The Parasite of Quartan Fever.

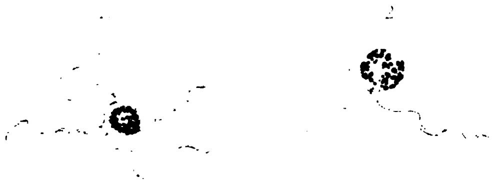


FIGS. 1–15 represent the phases of development and segmentation of the parasite of Quartan fever.



FIGS. 1–14 show the various forms of intra-corpuscular organisms in the **estivo-Autumnal** fever.

IV.



Two flagellate organisms.

There are several additional points of interest about the parasites:—

A corpuscle containing a half-grown organism may suddenly rupture; the hæmoglobin diffuses, and the pigmented parasite is set free. The parasite may break up into two or three portions; perhaps from pressure on the slide; and slight amœboid changes may be seen. In other instances, apparently from certain free extra-corpuscular organisms, the remarkable *flagellate form* develops itself. The pigment becomes more central, and the granules dance with great activity. Suddenly long, thread-like processes extend from the body of the parasite and display remarkable movements, thrashing about over the corpuscle with extraordinary rapidity (Fig. IV.) A flagellum may break off from the main body, and move about independently among the corpuscles. While these flagellate bodies appear in both the tertian and quartan fevers, they are very much more numerous in the irregular malaria. The significance of the flagellate form is still under discussion. A full discussion of the various views held regarding them is to be found in the monograph of Thayer and Hewetson. I do not agree with those who regard it as a degenerate form.

In the æstivo-autumnal fevers there is developed also a very striking body, to which much attention has been paid, the "crescent" of Laveran. In any case of irregular malarial fever, which has lasted a week or more, these bodies are to be found. They are developed within the red blood corpuscle, the margin of which may usually be seen on the concave surface of the crescent (Fig. V. 1 and 2). The border is very sharply defined, the protoplasm uniform, homogeneous with coarse pigment granules, often in the form of rods which are collected about the centre. Bodies similar in structure, but differing in form being ovoid and rounded, are also met with (Fig. V. 3); and one can trace the change of a crescent into an ovoid or rounded body, which, in turn, may in some instances be seen to project flagella and form a flagellated body similar to that derived from the extra-corpuscular organisms above referred to. Most authors say that both kinds of flagellated bodies do not develop unless the blood be exposed to the air, but an exposure of one or two minutes gives the best results (Ross). It would seem then that they do not exist as flagellate forms in the circulation.

Active phagocytosis goes on in all forms of malarial infection. The pigmented leucocytes represent the white blood corpuscles which have devoured the pigment, or more commonly the organism with the pigment in it. The flagellate bodies are almost constantly attacked by leucocytes.

The relation of these varieties of the malarial parasite to each other is still under discussion. Golgi, Marchiafava, and other Italian observers hold that they are distinct varieties, not interchangeable, though closely allied biologically. Laveran, on the other hand, contends for the unity of the forms, which he regards as modifications of one polymorphic parasite. Our experience in Baltimore strongly corroborates the views of the Italian workers; but with the present imperfect knowledge of the full life history of the parasite the question cannot be considered as settled.

Classification of the parasites.—Here, too, there is much uncertainty and corresponding discussion. A majority of authors place the parasites among the *Sporozoa* in the order of the *Hæmosporidia* of Danilewsky; others place them in the *Sarcodinia*, and speak of them as *Hæmamœbæ*. Until the matter is settled we can speak of the parasites as *hæmatozoa*, and use such names as *amœba*, *segmenting forms*, *flagellate bodies* and *crescent*, to specify the various forms assumed by the parasites.

Hæmatozoa in other animals.—Blood parasites are extremely common in cold-blooded animals and in birds. They may be best studied in the frog. Birds appear to suffer from a malarial infection similar to that in man. In one form the parasites develop themselves within the corpuscles and segment as in man.

The Parasite outside the body.—Considering the number of investigators at work upon the subject, it is strange that we are as yet ignorant of the form in which the parasite exists outside the body. The only observation bearing on the question is one of Grassi, who found encysted amœbæ in the nostrils of birds hung in cages in malarial regions, and subsequently found hæmamœbæ in their blood.

In another wide-spread disease produced by blood parasites—the Texas cattle fever—the hæmatozoa are conveyed from animal to animal by means of the cattle tick. It has been suggested that the mosquito may possibly be the carrier of the contagion, but of this there is no evidence.[1] As previously mentioned, the general opinion is that infection takes place through the respiratory tract.

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[1] If the crescent-shaped sphere be watched for some time, in many instances the pigment it contains is observed to become agitated, the body itself to undergo remarkable changes of form, and, finally, to throw out flagella just as happens in the case of the "free extra-corpuscular organisms" of the simple tertian and quartan parasites, as mentioned in the text. The crescent of the "æstivo-autumnal fevers" is, therefore, the homologue of the free extra-corpuscular organisms of the tertians and quartans. Arguing from the well-ascertained and very remarkable fact that neither of these forms of flagellate bodies are developed until the blood containing them has been for some time out of the body, Dr. Manson (*Brit. Med. Jour.* Dec. 8th, 1894) concludes that their function lies outside the body; in fact that their purpose is the continuation of the life of the malaria parasite outside the human body. As they take their origin from what was at one time an intra-corpuscular amœboid body, he regards the flagella as flagellated spores, the flagellum being provided for purposes of locomotion and penetration. Arguing, also, from the manifest inability of the crescent and "free extra-corpuscular bodies" spontaneously to leave the blood-vessels of man, from the known facts of the geographical and endemic distribution of malarial disease, from the close analogy in biological requirements between the malaria parasite and filaria nocturna, and from many other circumstances, Manson concludes that the mosquito is the agent which removes the malaria parasite from the human body and gives it the opportunity of continuing its existence as a species. He considers that malaria is very probably a disease of insects; the malarial organism being a gregariniform parasite capable of living in the body of man or in the body of mosquito—the hosts being interchangeable so to speak. This view is not altogether hypothesis. As a matter of fact, acting on Manson's suggestion, Surgeon-Major Ronald Ross, I.M.S., of Secunderabad, India, by feeding mosquitoes on the blood of malarial patients, has been enabled to trace the crescent body into the stomach of the mosquito, where it rapidly, and in almost every instance, passes through the ovoid, spherical, and flagellate stages, the flagellum finally breaking away and swimming about as if in search of some suitable nidus in

Inoculation experiments.—Since Gerhardt, in 1884, showed that malarial fever could be transmitted by inoculation, many confirmatory experiments have been made, chiefly by Italian observers. A full account of these is given in the monograph of Thayer and Hewetson. They are sufficient now to show that the disease may be transmitted directly from man to man. The period of incubation is from eleven to twelve days in the regular intermittents, and from two to five days in the irregular autumnal fever. In almost every instance the variety of organism introduced has been reproduced.

Correlation of symptoms with the life history of the parasite.—The remarkable clinical features of malaria—particularly the paroxysmal character of the attacks, the rapid anæmia, and the profound toxic features of the severer forms—find a ready explanation in what we now know of the mode of growth and action of the hæmatozoa.

The correspondence of the cyclical development of the parasites with the intermittency is one of the most interesting discoveries in pathology. The ague paroxysm is associated with the segmentation of enormous groups of intra-corpuscular amœbæ; and, as Baccelli suggests, the symptoms are probably due to toxines liberated during sporulation, or to substances set free in the blood by the rapid destruction of a large number of its corpuscles.

It has been shown that the toxicity of the urine is increased during the paroxysm; and the disseminated areas of necrosis which have been found in the organs of the body by several observers are similar to those produced by the soluble toxines of bacteria.

The anæmia is a direct result of the destruction of the red blood corpuscles, which are greatly reduced in number after each paroxysm. The melanæmia and the accumulation of the pigment in the liver and in the spleen and bone-marrow are secondary to this active destruction of the red blood corpuscles.

And lastly, the disappearance of the symptoms of malaria after the use of quinine is due directly to the parasiticidal action of the drug.

Morbid Anatomy.—The primary and the most important changes are in the blood. The condition of melanæmia has been recognised since 1847, when Meckel discovered the pigment. It results directly from the destruction of the red blood corpuscles by the parasites. The parasites themselves, as well as particles of free melanin, are taken up by the leucocytes. The blood is hydræmic; and, in cases of very intense infection with rapid destruction of corpuscles, there is hæmoglobinæmia, with tinging of the serum. In the melanæmia of chronic malaria the pigment accumulates in the spleen, liver and bone-marrow. The

which to bury itself—some cell corresponding to the human blood corpuscle in which its homologue—the spore derived from the rosette-body—buries itself in the human infection. Owing to the minuteness of the flagellum and other difficulties, the progress of the parasite in mosquito has not as yet been traced further; but that development to the extent described does take place in mosquito is certain, and is attested by numerous microscopic preparations now in England. Ross says he has succeeded in giving malarial fever to healthy men by administering to them water in which malariated mosquitoes had died.—Ed.

opportunities for studying fatal cases of simple intermittents are not very common. In a case of death by accident in the second week of this malady the spleen was enlarged (weighing 800 grammes), diffluent, and very dark red in colour. The liver weighed 2000 grammes; the surface was smooth, and the substance of a dark brown colour. In cases of long standing the liver and spleen are firmer, and show pigmentation, particularly about the capsule and in the fibrous trabeculæ. The malarial parasites are readily recognised in the blood corpuscles within the capillaries. They are very unequally distributed in the different forms. During life the quartan and tertian varieties are met with in large numbers in the circulating blood; while the æstivo-autumnal variety is found chiefly in the spleen, bone-marrow, and liver. In the organs the parasites are found most abundantly within the capillaries, particularly along the walls of the larger veins. Active phagocytosis goes on in the blood, the mono- and polynuclear leucocytes being the most active agents. The statement of Metschnikoff that the endothelial cells of the capillaries, especially of the liver, take up the parasites, has been corroborated by Barker. The macrophages of the spleen play a very important part, and Kupffer's cells of the liver also show much pigment. Recent studies have also shown two important changes which are well brought out in Barker's study of the fatal cases from my wards; namely, the occurrence of areas of necrosis in the spleen and liver very similar to those which occur in diphtheria and in typhoid fever. In the liver these may represent the primary change which leads to cirrhosis. In both acute and chronic cases thrombosis of the capillaries is met with in the brain, and in the spleen, liver, kidneys, stomach, and intestines. The lesions in the intestines, described by Barker, are of especial interest; as upon them probably depend the severer symptoms in the gastric and intestinal types of pernicious malaria. On this point Barker states: "When we consider the many variations possible in the implication of the capillaries in any organ, the diversity of the disturbances of the cerebral functions observable clinically becomes easily understandable. It is not difficult to conceive that herein may lie the key to the transitory aphasias, the variation in degree, extent, or duration of the paralyses, or of the mental irregularities occasionally noticeable in the severer forms of æstivo-autumnal fever; and when, along with other things, we remember that comparatively limited disturbances of the circulation in certain of the vital centres, such as the medulla, suffice at times to cause sudden death, it is not surprising that the type of malarial infection which is associated with the possible occurrence of the capillary thrombi of parasites should have won for itself the title of *malaria perniciosa*."

In malarial cachexia the anæmia is profound. The spleen is greatly enlarged, weighing from seven to ten pounds; is firm, and cuts with resistance; the capsule is thickened, and the parenchyma is brownish or yellow brown, with areas of deep pigmentation. In very protracted cases the organ is extremely melanotic, particularly in the trabeculæ and about the vessels. The liver may be much enlarged, but the increase in size is moderate in proportion to that of the spleen. The amount of pigment diffused throughout it gives a slate colour to the section; varying with the duration of the disease, the shade is from a light gray to a deep slate gray: beneath the capsule and surrounding the portal vessels there is a deep impregnation with melanin. The kidneys are enlarged, grayish red in colour, and areas of pigmentation may be seen in them. The peritoneum is usually of a deep slate colour; and the mucous membrane of the stomach and intestines has the same hue. The brain cortex shows a deep reddish gray colour, or in very chronic cases a dark slate gray or a chocolate brown. In some of the comatose cases the capillaries of the gray matter are stuffed with red blood corpuscles containing the parasites.

Symptoms.—*Incubation.*—As mentioned above, the symptoms follow exposure at a variable period—from three to five days in the irregular, and from ten to twelve days in the regular malarial fevers. In very malarious regions new-comers may be seized with the intermittent fever within a few days after their arrival. On the other hand, there are remarkable cases in which a person has dwelt for a long time in a malarious district without manifesting any symptoms, and yet on removal to another country has had several paroxysms of intermittent fever. There are instances, too, in which the process seems to be latent throughout; and a person may dwell for years in an infected region without having paroxysms or, indeed, fever of any sort; and he may then come under observation for the first time with anæmia and a greatly enlarged spleen and liver.

A satisfactory classification of the various forms of malarial fever is difficult to make. It is, perhaps, best to consider them under the primary subdivisions of regular and irregular malarial fevers; the former embracing the true intermittents, and the latter the remittent and continuous fevers: in a third subdivision may be considered the after effects of the infection; namely, the malarial cachexia.

I. Regular malarial fevers.—*Intermittents.*—There are two important types, the tertian and the quartan.

Tertian Fever.—This is the common infection in temperate climates. In the single tertian the paroxysm recurs at the end of forty-eight hours; in double tertian there is a paroxysm at the end of every twenty-four hours — quotidian. Of 339 cases in which the typical tertian organisms were present, there were 151 cases of single infections with a paroxysm at the end of forty-eight hours, and 188 double infections with a paroxysm at the end of twenty-four hours.

The tertian infection can be readily recognised by the appearance of the intra-cellular amœbæ and the method of their segmentation. In a large proportion of the cases the paroxysms are very regular in form; thus of 116 cases showing infection with two groups of tertian organisms, 114 had characteristic quotidian paroxysms. Variations from the regular form are rare, and consist chiefly in abortive paroxysms, or in an irregularity of the course of spontaneous disappearance. In a few instances of infection with the tertian organisms the temperature was irregular, with a slightly remittent character, for a week.

That the quotidian intermittent is due to the action of two groups of the tertian parasite (or three groups of the quartan) is shown not only by the blood examination, in which the two sets of organisms can be distinguished at different periods of their development, but also by the temperature curves which indicate that the chills of alternate days are similar in the hours of onset. A dose of quinine given just before or early in a paroxysm will destroy the products of segmentation of the group of organisms which has to-day reached its development; but the half-grown set of to-morow's paroxysm will not be influenced. Thus a case of quotidian fever is not infrequently changed into one of tertian after admission to hospital. Quotidian intermittent fever may also be associated with the æstivo-autumnal parasite; but there are marked differences in the paroxysms, which are longer, averaging twenty-one hours: in one instance they lasted thirty-eight hours.

Quartan intermittent fever is rare in this latitude. There were only five out of a total of 616 cases examined during the first five years at the Johns Hopkins Hospital. Two of these were single infections with the paroxysm at the end of seventy-two hours, and three were triple infections, in which there was a paroxysm every day. There was no instance of double quartan, in which there is an interval between two successive paroxysms. As I have said, the quartan form of the parasite is readily recognised.

Phenomena of the attack.—The ordinary paroxysm is divided into three periods—the cold, the hot, and the sweating stages.

The *cold stage*.—At the onset the patient feels tired, stretches himself frequently, yawns, has slight headache, uneasy sensations in the epigastrium, and sometimes nausea and vomiting. At this stage the temperature has already risen. In a little while the patient begins to feel cold, and soon to shiver, and he seeks the fire, or covers himself with the bed-clothes. The face looks cold; the tip of the nose, the lips and the fingers are blue, and, in the fully developed rigor, the whole body shakes, the teeth chatter, and the movements may be violent enough to shake the bed. Not only does the patient look cold and blue, and feel cold, but the surface thermometer indicates a reduction of the skin temperature. On the other hand, the rectal temperature during the chill may reach 105° or 106°.

Of other symptoms associated with the chill, nausea and vomiting are very common. The headache is often intense; the pulse is small and rapid; the urine is increased in quantity. The chill lasts from twenty minutes to an hour; sometimes in very severe paroxysms for two hours or yet longer.

The *hot stage* is ushered in by flushes of heat, and gradually the coldness of the surface disappears; the shivering ceases, and soon the skin becomes intensely hot and dry. The contrast in the patient's appearance is very remarkable. The face becomes flushed, the hands are congested, the general surface is reddened, the heart's action is forcible, and the pulse is full and strong. The headache becomes aggravated, and is of a very throbbing character. Epistaxis may occur. The temperature may not reach its height until this stage, though as a rule by the end of the chill the fastigium has been reached. The hot stage lasts from an hour to three or four hours. With high fever the patient may become actually delirious; and a few years ago a man in such a state sprang out of bed and jumped through the window of the ward.

The *sweating stage* begins with the appearance of moisture of the skin, and gradually the whole body is bathed in a profuse perspiration. The headache is relieved, all the uncomfortable feelings pass away, and the patient sinks into a refreshing sleep. The urine passed in this stage is usually dark in colour, and deposits a copious sediment of urates.

The total duration of the paroxysm is remarkably uniform in the regular intermittent fevers. The average duration of the paroxysm in our single and double tertian cases was 11·8 hours. In the large number of cases which we have examined, taking two hourly observations, the uniformity in the duration of the paroxysm is somewhat remarkable, and contrasts with the intermitting fever of septicæmia.

One or two additional points may be mentioned. In children convulsions sometimes occur. Herpes is very frequently seen; urticaria is not uncommon, and a general erythema occurs sometimes. Bronchitis is not uncommon at the onset. Albuminuria was present in 133 of 333 cases in my wards; and the toxicity of the urine is increased after the paroxysm. The spleen may enlarge, and a soft bruit may be heard over it. Orchitis has been noted by several observers, who did not prove, however, by microscopical examination of the blood, that the associated fever was certainly malarial.

During the paroxysm and before it, segmenting forms, or the products of segmentation, are to be found; if it be a double tertian—that is, quotidian—the half-grown organisms of the next day's paroxysm will be found also.

Time of recurrence.—The recurrence of the paroxysm is usually at the same hour on the succeeding day in double tertian, or on every other day in a single tertian. As the disease progresses there is often a tendency to anticipation; in other cases there may be retardation or postponement. These variations are of great interest, and by the older observers were anxiously looked for; as the former was thought to be a bad sign, and the latter a favourable one. It is rare in simple intermittents for the paroxysms to succeed each other with such rapidity that the one is not over before the other begins. An intermittent of this type was spoken of formerly as *subintrant*. The paroxysms recur most frequently in the morning hours or about noon. Late afternoon and evening chills are rare.

If not treated, simple intermittents disappear spontaneously, recur, or become chronic; in a few instances the disease assumes the pernicious character. Spontaneous disappearance is by no means uncommon. Of 58 cases of tertian infection, 11 showed a spontaneous disappearance of the fever after admission, and in 3 of the 47 remaining cases the fever disappeared after one or more paroxysms without the administration of quinine. In such cases recurrence is almost certain, and in a few weeks or a month the chills reappear. If not properly treated the patient becomes very anæmic, the spleen enlarges, and a condition of malarial cachexis supervenes. In temperate regions it is rare to see pernicious symptoms in simple intermittents. No such instance has occurred in our cases; but in the tropics hæmorrhagic features or coma may appear in the course of simple intermittents.

II. **Irregular malarial fevers.**—The spring and early summer infections are ordinary intermittents; the late summer and autumn infections, even in temperate regions, are characterised by a large number of cases more irregularly intermittent, of continuous and remittent fevers, and of the graver, more pernicious types which occur at this season alone. The Italian observers have shown that with these forms there are differences in the parasite; there is not a regular periodic segmentation in the blood, but the process occurs in the internal organs. Laveran's crescents are developed, and the flagellate organisms are more common.

(*a*) *Irregular Intermittents.*—That the autumnal are less definite than the spring agues is a very old observation; the paroxysms are longer, often lasting eighteen or twenty-four hours; they tend to approach each other, and by coalescence we may get an almost continuous pyrexia with perhaps a pseudo-crisis. Of 105 cases in which the æstivo-autumnal parasite of the Italians was present, there were 38 with quotidian, 6 with tertian paroxysms, and 38 with continuous fever, or with paroxysms which tended to become continuous.

(*b*) *Continuous and Remittent malarial fevers.*—The disease may set in with a violent chill, but is very often preceded by headache, nausea, vomiting, and aching pains in the back and limbs. Chilly sensations may occur for several days. The gastric symptoms may be very well marked—such as nausea and urgent vomiting, often of a yellow green bilious material. The fever may be continuous, with daily remissions, which may be very slight; while in other cases with irregular fever a two-hour temperature chart will show distinct intermissions. After the onset chills are not common. The general appearance of the patient is often strongly suggestive of typhoid fever, and without a blood examination it may be impossible at first to make a diagnosis. In some instances a slight hæmatogenous jaundice develops early.

The cases vary greatly in severity. The fever subsides at the end of a week, or it may persist for fourteen or sixteen days. In the severer forms delirium may occur, and pernicious symptoms, such as coma or hæmorrhages, may develop themselves. Though at the outset these cases may resemble typhoid fever very closely, and on admission the flushed face, the furred tongue, and the enlarged spleen may lead to an error in diagnosis, the more irregular character of the fever (particularly during the first week at the very time when the pyrexia of typhoid fever is most steady), the early anæmia, and the greater enlargement of the spleen, are suggestive features. The blood examination is of the greatest importance, and upon it alone the diagnosis may rest. The organisms, which in mild cases are often very scanty, are of the third variety above described, the æstivo-autumnal forms of Italian observers. The hyaline bodies are more ring-like, and as they are developed the stroma of the corpuscle has a curious brassy green appearance, and looks shrunken; segmental forms are rarely seen, and within five or six days the ovoid and crescentic bodies are found. In this group come the cases of gastric remittent, bilious remittent, and typhoid remittent of various authors.

(c) *Pernicious malarial fevers.* — These have become very rare in temperate climates; of the 616 cases which were under observation at the Johns Hopkins Hospital during the first five years of its work, there were only three instances of this type, two of which terminated fatally. The following are the most important forms:—

The *comatose form*, in which the patient may be struck down with symptoms of the most intense cerebral disturbance, such as acute delirium or, more frequently, a rapidly increasing coma. The attack may be preceded by a chill, or by one or two paroxysms of intermittent fever. The unconsciousness may persist for from twelve to twenty-four hours, and the patient may die in the coma. After regaining consciousness a second attack may come on and prove fatal. The number of organisms found in the blood may be small. It should be borne in mind that while the temperature in these cases may be elevated at first, it often falls on the second or third day, and may become subnormal. The comatose and apoplectic forms are not confined to the æstivo-autumnal type, but may occur with the tertian infection.

In the *algid form* of pernicious malaria the attack begins with gastric or gastro-intestinal symptoms; the vomiting is urgent, and there are sometimes cramps in the abdomen and frequent mucous or watery stools: in some cases there may be choleriform attacks. The patient complains of cold, though he may not have actual chills. The temperature may be normal or even subnormal; the pulse is feeble and small; the respirations are increased. The urine is often diminished or suppressed. In a case admitted on 10th September 1890, the man had had no chills, but had been ill since the 7th. When first seen he was prostrated, extremely feeble, could not give a rational account of himself, and looked as if he had been drinking. There was no alcoholic odour of the breath, and on learning that he had recently come from Savannah, I at once made an examination of the blood, and found a large number of the small ring-shaped intra-corpuscular parasites. During the next five days, in spite of the energetic use of hypodermics of quinine, the patient remained depressed and prostrated, the vomiting persisted, and the temperature sank, so that on the 15th and 16th it was only between 95° and 96°. This type is essentially the same as that described as the *asthenic* and *adynamic*.

Hæmorrhagic malarial fever.—In all the severe types of malarial infection hæmorrhage may occur from the mucous membranes. It is most commonly met with from the kidneys, and is either a hæmaturia or a hæmoglobinuria.

Malarial hæmaturia occurs in epidemic form in certain districts, and is often known as bilious hæmorrhagic fever. The renal symptoms may be the sole manifestations, or they may follow paroxysms of ague. In the severer cases there are all the symptoms of an intense infection,—vomiting, nervous symptoms, and a hæmatogenous jaundice. Death usually follows in course from suppression of the urine. [*Vide* art. "Blackwater Fever."]

III. Malarial cachexia.—If a patient with chills and fever for several weeks be improperly or insufficiently treated, in a month or so the disease recurs, and the attacks may be repeated through a period of many months, until the subject presents the two distinguishing features of malarial cachexia, namely, anæmia and an enlarged spleen. It is very rare in this latitude to meet with cases which have developed themselves without chills or febrile paroxysms; but dwellers in very malarial districts may fall into the cachexia without, to their knowledge, having had fever. They are said then to have suffered from the "masked" form of the disease. In this latitude the most severe cases of this kind come from Central America and from the West Indies. The anæmia, which is due to the direct destruction of the corpuscles by the parasites, may be very intense—from 1,000,000 to 2,000,000 red corpuscles per cubic millimetre. The general characters are those of a secondary anæmia. The leucocytes are usually diminished. The general features of the anæmia are extremely well marked; the colour of the skin is saffron yellow, or of a lemon tint, not often the light yellow of pernicious anæmia, but a darker, dirtier, more muddy yellow. Shortness of breath, œdema of the ankles, and hæmorrhages are common, particularly into the retina. The spleen is greatly enlarged, hard and firm: it may reach as low as the crest of the ilium, or it may fill the left half of the abdomen. The subsequent history of these cases of very chronic malarial cachexia is of interest. When the condition has not lasted very long, removal from the infected district, together with the use of quinine, iron, and arsenic, may quickly cause the anæmia to disappear; and the spleen may be gradually reduced in size. Serious accidents, such as hæmorrhage from the stomach, may occur and prove fatal. In other instances the anæmia gradually disappears, but the "ague-cake" remains in spite of all treatment. After persisting for some years great reduction in this organ may occur, but I have never seen the enormous spleen of chronic malarial cachexia, reaching for example to the pubes, restored to its normal size.

Complications and Sequels. — *Dysentery* and malaria not infrequently coexist. In this latitude, however, the association is rare. Entero-colitis occurred in only two, and amœbic dysentery in one of the list of cases already mentioned. In campaigns in very malarious districts the two diseases have been often found together.

Pneumonia.—It was formerly believed that an especial form of pneumonia was caused by the malarial poison. This idea is now exploded, and the Italian observers have proved by bacteriological examination that, as in other forms of pneumonia, the micrococcus lanceolatus is present. Pneumonia appeared in two of the cases which have been under our observation. In neither case did the disease show anything remarkable in its course, or indicate that the malaria exerted any influence upon the progress of the disease. It is interesting to note that the action of quinine may cause the disappearance of the malarial parasites without influencing in any way the temperature of the pneumonia.

Typhoid fever may run concurrently with malaria. No instance has occurred in our series, though one patient, admitted on 16th October with malaria which yielded readily to quinine, developed the typhoid fever on the 22nd; he probably had a double infection on admission. The cases of so-called typho-malarial fever are usually enterica.

The changes in the liver in malaria have attracted the attention of observers for many years, and the relation between *cirrhosis* and malaria has been much discussed. Dr. Barker, in his study of fatal cases of malaria, found extensive areas of necrosis in the liver similar to those which can be produced experimentally by blood serum. He states that "the malarial pigment tends to accumulate in the periphery of the hepatic lobules and in the trabeculæ of the spleen. It remains, too, for some time after the infection has disappeared; and it is not impossible that the irritation caused by the presence of this pigment might give rise to a chronic interstitial inflammation, a result perhaps analogous to the pneumonoconioses. It seems less probable, however, that the pigment is responsible for a new growth of fibrous tissue than that the latter is secondary to a degeneration due to toxic effects." Certainly in this latitude a cirrhosis which can be reasonably attributed to malaria is extremely rare. We have had but one case clinically in which the association seemed to be quite clear. Kelsch and Kiener have described several varieties of malarial cirrhosis, but that they are all due to paludism is by no means certain.

Diagnosis.—Since Laveran's studies the diagnosis of malaria in all its forms has been greatly simplified. The parasites which in all its forms are present in the blood in varying numbers require a proper technique and a certain experience for their recognition.

Two serious errors in diagnosis may be made. Paroxysms of an intermitting fever, which are common in other diseases, may be mistaken for those of malaria; or, in one of its protean manifestations, the graver form of malarial infection may be overlooked.

The early stages of tuberculosis, of ulcerative endocarditis, of suppuration in various parts associated with septicæmia or pyæmia (among which may be mentioned particularly affections of the bile passages and abscess of the liver), and of pyelitis, are among the affections most commonly mistaken for malarial intermittent fever. There are three points of distinction: first, the septic paroxysm is rarely so regular; sometimes it extends over fewer hours, but more commonly over a longer period, and it rarely returns with the same punctuality. In the simple intermittents the duration of the paroxysm is almost invariable—between eleven and twelve hours. Secondly, the examination of the blood in the septic paroxysms shows an absence of the malarial parasites, and of melanæmia, and the presence of a well-marked leucocytosis. Thirdly, malarial intermittent fever is invariably controlled by quinine. An intermitting fever which resists quinine, even for three or four days, is not a malarial fever.

In regions in which pernicious malarial fevers occur, practitioners are of course on their guard, and learn to recognise the very anomalous symptoms with which the disease may set in. The comatose form, which may set in with great suddenness, may be mistaken for sunstroke or apoplexy. The gastro-intestinal form may suggest a severe attack of simple indigestion, or an attack of cholera nostras. The hæmorrhagic forms are more readily recognised: a careful blood examination in these cases settles the diagnosis at once; these cases are usually associated with the æstivo-autumnal type of organisms. In some of the cases the parasites are chiefly in the spleen, liver and bone-marrow: the blood withdrawn directly from the spleen may show large numbers, although in the circulating blood they may be very scanty. Before puncture it is well to give at the site a small hypodermic injection of cocaine in order that the patient may not give a sudden lurch; for in the acute splenic tumour the procedure is not without risk. I have heard of an instance in which by a spleen puncture a superficial rent was made in the capsule through which the patient bled to death.

The separation of the continued and remittent malarial fevers from typhoid fever is now rendered easy by the blood examination, which should be a routine practice in all fever cases in malarial regions. The general appearance of the patient, the furred tongue, the apathy, even the preliminary bronchitis, may suggest typhoid fever very strongly; but, as I have said, the fever of the first week of continual malarial fever is never so steady as in typhoid, and in the latter disease the rapid anæmia is never seen.

Prognosis.—In temperate climates the prognosis is good. Unfortunately for many years and in many regions practitioners have been in the habit of labelling as malaria every instance of obscure disease in which they could not make a diagnosis; so that the vital statistics are falsified in a remarkable manner. In the United States Census Report for 1890, which covers the six preceding years, the deaths from malarial fever in New York and in Brooklyn were more numerous than from typhoid fever. In both these cities it is notorious that a death from true malaria is a great rarity, not more than three or four cases occurring each year in the entire hospital practice of the city of New York.

It is to be hoped that one practical result of Laveran's observations will be a much greater accuracy in the returns of mortality.

In the regular forms of malarial fever the death-rate is very slight, and results usually from complications, such as acute nephritis. I have mentioned one case in which, during the delirium of the paroxysm, the patient jumped through the second story window and received injuries from which he died.

Under favouring conditions malaria is one of the most fatal of all known diseases. In certain campaigns, as in the ill-fated Walcheren Expedition, it has proved a terrible pestilence. The mortality in hospital work in this locality is only about one per cent, and the mean mortality from the disease in the community is probably much lower.

Prophylaxis.—Thorough drainage and systematic cultivation are the two measures by which malarial districts have been rendered healthy. The rapidly-growing eucalyptus tree has been found very useful, probably through its influence in draining the soil. In malarious regions it is safer to boil the water used for drinking purposes; though, as already stated, direct experiment is opposed to the view that malaria is a water-borne disease. Persons travelling in infected countries should avoid the night air, and rest carefully during the hotter portions of the day. In unsettled regions, and during expeditions, the greatest care should be exercised in the selection of camps, and positions as high as possible should be occupied; travellers believe that large fires have an important prophylactic influence. It is well not to sleep on the ground. Quinine may be used as a prophylactic, and the evidence is strongly in favour of its beneficial effect. At first as much as half a drachm may be taken in the day, and then smaller quantities.

Treatment.—This is comprised in one word, *quinine.* The introduction of cinchona into Europe two hundred and fifty years ago ranks not only as one of the greatest events in the history of medicine, but as one of the great factors in the civilisation of the world. The drug remains to-day, in its potent action on the malarial poison, the ideal medicine; and, repeating the words of Sydenham, used more than two hundred years ago, we can say that it is *absolutum specificum.*

Action of quinine on the parasites.—Binz suggested, in 1867, that quinine probably acted as a protoplasmic poison on the infective agent of malaria; and since the discovery of the amœba a number of observations have been made to determine the effect of this drug on the organism. Laveran showed that a solution of $\frac{1}{10000}$ of quinine, run under the cover-glass, would check at once the movements of the amœba. As, however, a like effect is produced either by the water or by the salt solution in which the quinine is dissolved, we meet with an almost insuperable difficulty in the study of the direct action of the drug upon the parasites themselves.

Many careful studies have been made upon the effect of quinine on the parasites circulating in the blood; and some such effects have been described by Golgi and others, particularly a diminution in the activity of the amœboid movements. Some years ago I made careful hourly examinations in a series of cases with a view of ascertaining, if possible, the direct influence of full doses of quinine; but I could not make up my mind that any particular change was to be noticed in the intra-corpuscular tertian parasite while undergoing destruction by the specific. In dried preparations, however, several authors have noted loss in the staining property of the organism.

Nevertheless three points about the action of quinine on the parasites are well established.

First, That under its use the intra-corpuscular varieties, whether tertian, quartan, or æstivo-autumnal, rapidly disappear from the circulating blood.

Secondly, That quinine administered some hours before a paroxysm will not interrupt the cycle of their development, but will usually destroy the products of segmentation, and so check the succeeding paroxysm.

Thirdly, That the crescentic and ovoid bodies which develop in the æstivo-autumnal fevers are very slightly affected by the action of quinine.

Treatment of the intermittent malarial fevers.—During the paroxysm measures should be taken to make the patient as comfortable as possible. In the cold stage he desires plenty of external heat and warm drinks; in the hot stage he desires just the opposite. The irritability of the stomach and vomiting may seriously interfere with the taking of liquids. It very rarely happens that the collapse of the cold stage is at all dangerous, but in the debilitated it may be necessary to administer warm stimulants. One of the most comforting procedures in the early period of a chill is a hypodermic injection of morphia. If the fever run very high the patient may be sponged in the hot stage; it is rarely worth while to resort to the antipyretics. Occasionally a patient becomes actively delirious during the paroxysm of intermittent fever, and if possessed with the idea that he is being persecuted, may injure himself in his attempts to escape.

The specific treatment consists in the administration of quinine in doses sufficient to destroy the parasites. The time of administration in simple intermittent fever makes very little difference. Sydenham advised its administration after the paroxysm. Given at this time an efficient dose will usually destroy the products of segmentation, and prevent the chill which will be associated with their development. For instance, in a double tertian, if immediately after to-day's chill quinine be given, it will not destroy the half-grown parasites in the blood corpuscles which will cause the chill to-morrow, but the patient almost positively will not have a chill on the succeeding day. Golgi and most of the Italian observers think that the quinine is best administered several hours before the paroxysm is due, so that it is in solution in the blood at the time of the setting free of the spores. Dock, on the other hand, prefers to give it between the paroxysms, when the amœboid phase is most active. The amount of quinine required to check a simple intermittent is very small. I have often demonstrated to students that one grain three times a day in a simple tertian fever will prove effective. In general practice it is perhaps better to give during the first two days of treatment as much as twenty or thirty grains of quinine in the twenty-four, and then gradually lessen the amount. Recurrences are extremely common; and they are not always reinfections. When a person has had ague it is of some importance to keep up the use of the quinine in moderate doses, for some months. The sulphate and the hydrochlorate are the salts in common use; and they are best given in solution or in cachets. The old standard mixture of quinine and aromatic sulphuric acid is perhaps the most satisfactory, except for children. When quinine given in solution does not check an intermitting fever the practitioner may know that he is not dealing with the kind due to the malarial parasite.

In the irregular malarial fevers quinine is equally efficacious; and in the cases with remittent or sub-continuous types of pyrexia the fever usually disappears within a day or two. In the pernicious types of the disease—particularly the comatose, the algid, and the hæmorrhagic—as soon as the character of the disease is recognised, the patient should be thoroughly cinchonised. It is usually impossible to do this by the mouth, owing to the incessant vomiting; so that the drug must be administered subcutaneously, either the bisulphate in thirty-grain doses, with five grains of tartaric acid, or the soluble lactate or hydrobromate of quinine.

Hypodermically the drug acts more promptly, but is not any more effective than by the mouth. In many of the severer forms of fever the life of the patient depends first on a prompt diagnosis, and next upon the rapidity with which he is put under the influence of quinine.

There is a fixed belief in parts of the Southern States that malarial hæmaturia is due to the administration of large doses of quinine. So far as I have been able to judge from the recent records on the subject, the evidence upon which this statement is based is very far from sufficient. Personally, too, I can say that using quinine in very large doses, as I often have done, I have never met with an instance in which it caused hæmaturia. On the other hand, in instances of acute albuminuria and of acute hæmaturia in malaria, I have seen the prompt and beneficial action of the drug.

Accessory measures must be employed in these serious cases: external warmth or the hot bath, hypodermic injections of ether, strychnia, and brandy, and the administration of food per rectum.

Malarial cachexia.—The milder forms improve rapidly with iron, arsenic, good food, and fresh air. Cases not of the chronic recurring type usually do well; but the patients who come under observation with great enlargement of the spleen and liver, the blood hydræmic, and the red corpuscles below one million per cubic millimetre, may resist all medicinal and hygienic measures, and die with the symptoms of a progressive anæmia. Some of the most desperate cases recover so far as the blood condition goes, but the spleen remains enlarged, forming a chronic ague-cake which is very difficult to reduce. External applications, such as the biniodide of mercury ointment and iodine, are recommended. The direct injections of arsenic into the spleen have been advised; I used it persistently in three cases without any benefit. In some of these patients the spleen is so hard and indurated in its chronic hyperplasia that very little change can be expected; though in the course of years it may slowly diminish in size.

Quinine is of very little service in the malarial cachexia, as in the advanced cases the parasites are no longer present.

I have not mentioned other remedies, such as methylene blue, eucalyptus, and the score of supposed antiperiodic remedies, which from time to time have been introduced. The physician who at this day cannot treat malarial fevers successfully with quinine should abandon the practice of medicine.

William Osler.

REFERENCES

For the voluminous bibliography of Malarial Fever, the reader is referred to the first of the three works cited below :—

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W. O.

HÆMOGLOBINURIC FEVER

Synonyms.—*Blackwater fever, Bilious remittent fever, West African fever.*

Definition.—These alternative names have been applied to a specific non-contagious fever, generally believed to be malarial in kind, which is accompanied by the presence of blood pigment in the urine.

Geographical distribution.—Hæmoglobinuric fever is practically confined to the tropical and subtropical regions of Africa and America, where within certain latitudes it is endemic. It occurs in its most virulent form in Equatorial Africa, decreasing in intensity both to the north and south of this portion of the globe. Curiously enough, however, the disease is much commoner on the West than on the East Coast of Africa. To so great an extent, indeed, is this the case that the term West African fever is not unfrequently employed as a synonym for hæmoglobinuric fever.

It is specially prevalent on the Gold Coast and in the Gaboon district.

Bérenger-Féraud, indeed, estimates that of the Europeans residing at certain French settlements in these regions no less than 38 per cent are annually attacked with hæmoglobinuric fever. On the Upper Senegal, also, the disease exhibits an attack rate almost as high.

Many cases have been reported from the Congo Free State, from the Cameroons, and from the Niger district; as well as from Sierra Leone, Cape Coast Castle, and other British settlements in this part of the world. The disease is, however, more common on the Congo and on the deltas of the Niger and Gambia rivers than in the sea-coast towns higher up the coast; but it is also known in the "Horn of Africa," where there are no large rivers. Officers of the French Medical Service have met with hæmoglobinuric fever in Madagascar.

On the East Coast of Africa the incidence of attack does not appear to be so great; although there the disease is by no means unfrequently met with, especially on the Zambesi.

At Zanzibar it appears to be unknown.

Attacks of hæmoglobinuric fever have also been known to occur at some considerable distance from the coast, as for instance in the Shiré Highlands, certain districts in Mashonaland, and other parts of Eastern Central Africa.

It has appeared now and again in Java and New Guinea.

A few somewhat doubtful cases have been reported from India, Assam, and Cochin-China, by Notter, Firth, Wenyon, and other observers; but in Asia the disease is practically unknown.

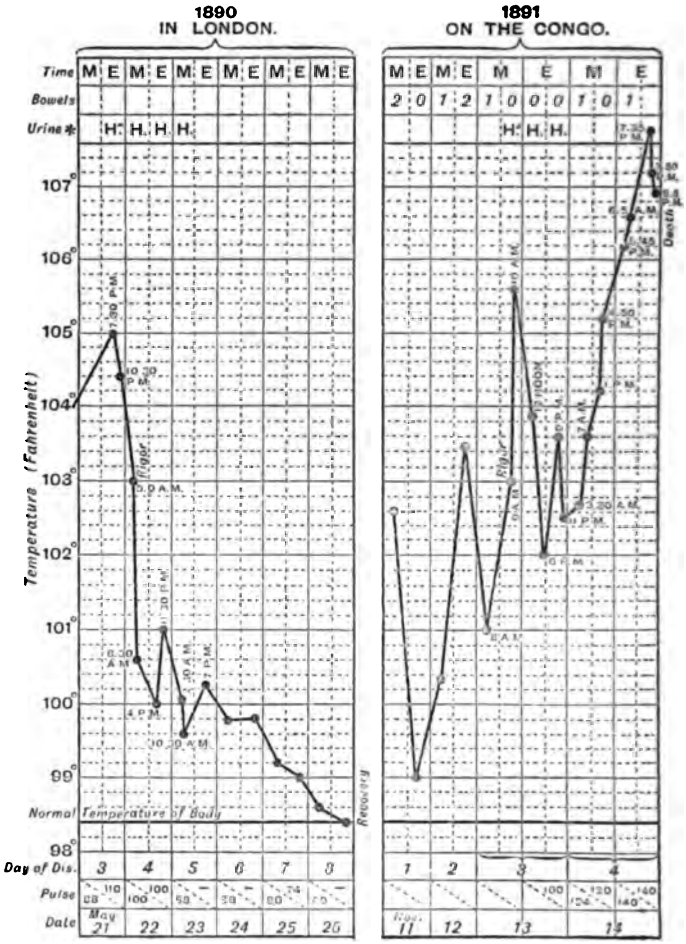
In America it occurs both in the northern and southern portions of the continent, as well as in the West Indian Islands. It appears to be specially prevalent in Cuba, and in the plains of Venezuela. In the highlands of this country, however, it is not common, and in Brazil it is never seen. In Europe a few cases have been reported from Italy and Greece.

It is an interesting point, and one worthy of note, that until comparatively recent years there existed no records of the occurrence of "blackwater" fever, even on the West Coast of Africa. Thus, in a report by Bryson on "Diseases of the African Station," which was published in 1847, there is no mention of the special symptoms so characteristic of this disease.

It is very difficult to account for this: for, although cases of the disease may have been less numerous fifty years ago than at the present time, yet it seems unlikely that this peculiar condition of the urine should have escaped notice altogether. It is possible that the colour of the urine may have been put down, in some instances, to the presence of bile, especially if the amount of pigment were so great as to render the urine quite black; but this error could hardly have been made in cases where the colour is of a more decidedly red tint, as it is when the urine is quickly extruded from the bladder, or when the attack is mild.

Battersby, Plehn, and others are of opinion that the disease has undoubtedly increased among Europeans; at any rate during the last few years. It is possible that disturbance of the soil, consequent on increasing cultivation of the land or its preparation for building operations, has brought about a wider dissemination or increased virulence of the poison. Careful observation of the varying meteorological conditions during a

CHART showing Course of Temperature, etc. during two attacks in the same person.



* H. *indicates the occurrence of hæmoglobinuria.*

series of years may throw some light on this interesting problem. Up to the present, however, such records are unfortunately not available.

Although blackwater fever never originates in non-malarial countries the clinical manifestations of the infection, as of other forms of malaria, may show themselves in non-malarial countries, and show themselves there perhaps for the first time. Thus attacks of blackwater fever may occur in England many months after the subject of them has left Equatorial Africa; and may even prove fatal. It would seem, however, that the liability to such attacks diminishes with lapse of time, and practically ceases after a prolonged residence in this country.

Causation.—This disease is met with both in natives and foreigners; but the negro races are for the most part less liable to attack than the European, although even negroes may suffer severely if removed to a locality at a distance from that in which they were reared. In any case the disease appears to occur only or especially in those who have previously suffered from malarial fever; while the individual paroxysms are excited for the most part by exposure to chill, severe heat, fatigue, excitement, starvation, or possibly, according to some observers, to indiscretions in diet.

Dr. Crosse states that blackwater fever hardly ever attacks old residents in West Africa if they have not suffered from it within two or three years of their visit to the country. According to this observer, it is also noticeable that blackwater fever seldom if ever comes on within the first year of residence on the coast, and it only attacks those who are anæmic and broken down by malarial poisoning. Cases are on record, however, in which the disease showed itself within a month or six weeks of landing in Africa.

Dr. Battersby considers that the two most important factors required for the production of the disease are heat and moisture: he presumes that the disease depends upon the invasion of the system by a micro-organism which has its normal habitation in the soil; and many virulent attacks after the turning up of virgin soil have been recorded. Almost equally remarkable, according to this observer, is the diminution of the disease which has been brought about in certain localities by drainage and cultivation of the soil. Thus districts previously malarial have been rendered more healthy. In regions where the disease is endemic it is a rule of practically universal application that low-lying river districts or land situated at the foot of hills are particularly unhealthy in this respect; while highlands are comparatively free from the disease.

It has been asserted that the specific poison may gain access to the system either through the medium of drinking-water or through the air. The exact nature of the poison, and, particularly, whether it originate in the vital activity of some bacterial or other form of organism, is unknown. Seeing, however, that the disease is generally believed to be of malarial origin, search has been made accordingly, in a certain number of instances, for Laveran's plasmodium malariæ; but at present the evidence of its presence in the blood of patients suffering from hæmoglobinuric fever is not so complete as could be wished. Dr. Andrew Davidson states that this parasite was associated with hæmoglobinuric fever in some cases which occurred at Rome; and Prout seems to imply that he met with malarial parasites in the blood of cases of this disease on the Gold Coast. Dr. Manson has put on record an account of two prolonged examinations of the blood of a patient, suffering from hæmoglobinuric fever, who came under his charge in London; the results were practically negative. As the patient had been drenched with quinine, Manson is of opinion that this is not to be wondered at. Crosse, I learn, has found the plasmodium in some cases; and Plehn gives a fairly full account of the particular variety of the parasite which produces blackwater fever or contributes to produce it. According to Plehn, the plasmodium belongs to the round unpigmented or slightly pigmented variety of the æstivo-autumnal plasmodium of the Italians. Smith and Kilborne, in 1889, showed that the so-called "Red-water or Texas Fever" of cattle is a disease of malarial affinity, and due to the presence of bodies in the red corpuscles of the blood which present a certain similarity to Laveran's parasite.

On the whole, the evidence appears to be in favour of regarding Laveran's parasite as intimately connected with this disease; but the peculiarities of its clinical features and geographical distribution suggest that blackwater fever is either caused by some peculiar form of the plasmodium, or that some factor, as yet unknown, is added to ordinary plasmodial invasion.

Symptoms.—A typical attack of hæmoglobinuric fever is usually ushered in by an initial stage of shivering, which may increase into a series of severe rigors. There is a sense of numbness in the extremities, intense pain in the loins, and general *malaise*.

The temperature rapidly rises to 103° F. or thereabouts, mounting at a later period to 105° F., or even higher; and dark-coloured urine is passed from the bladder. This is usually scanty in quantity, thick in consistency, and of high specific gravity. There is frequent desire to pass water, but increased effort is required to void the thickened urine; the act of micturition indeed may be difficult to accomplish, and accompanied by considerable pain. Frequent retching, attended in nearly all severe cases with bilious vomiting, is a distressing symptom which tends to exhaust the patient—this persistent vomiting of green bile being almost invariably present in cases tending to a fatal termination. Tympanites is a common and distressing symptom. At an early stage a more or less intense jaundice becomes rapidly established, the conjunctivæ and the skin over the entire surface of the body becoming of a bright yellow colour. Such coloration, however, is in all probability due not so much to staining of the integument with bile, as with disintegration products of hæmoglobin which, owing to the extensive hæmolysis which is one of the most marked features of the disease, are present in great quantity in the circulation. A considerable portion of the hæmoglobin and its derivatives, thus set free in the blood-stream, are eliminated by the kidneys; and it is to their presence in the urine that its peculiar colour is due. In all probability the proteid, which is often present in such quantity that the urine becomes absolutely solid when heated, is derived from this source also; since, as is the case in the urine of paroxysmal hæmoglobinuria, it consists for the most part of globulin. Formerly the colour of the urine appears to have been attributed to the presence of bile rather than of hæmoglobin; but this opinion is now known to have practically no foundation in fact, for bile is either entirely absent from the urine, or is present in an insignificant amount. The considerable pain over the region of the kidneys, which not unfrequently gives rise to much complaint, may be due to some congestion of those organs; and without doubt actual nephritis is occasionally set up as the result of the great elimination of hæmoglobin which takes place. This complication may be suspected if examination of the urine show that serum-albumin rather than globulin is present to any large extent. A concomitant nephritis, no doubt, also explains the fact, which has been reported by several observers, that actual hæmaturia, usually following on a previous hæmoglobinuria, has been known to occur in cases of this disease.

Frequently also there is much pain in the region of the liver and spleen, and these organs are enlarged.

The fever, which becomes somewhat marked at the very beginning of the paroxysm, may be remittent or almost continuous in course. Usually, however, after a longer or shorter interval the temperature drops somewhat, and the patient falls into a profuse perspiration. If so, all the various painful symptoms tend to abate; but an intense feeling of weakness remains. Coincidently with the subsidence of the fever the urine gradually begins to flow more freely and loses its dark colour, reverting, perhaps, after a time to its normal condition.

The paroxysm may now cease as suddenly as it began, but usually the temperature shortly rises again; rigors, and pains in the loins and over the liver return, while the urine probably once more becomes scanty and red or almost black. This series of events may recur several times in succession, with or without concurrent hæmoglobinuria. In the severer class of cases the symptoms persist without any apparent intermission, the urine becomes more and more scanty, and eventually may be altogether suppressed; under these circumstances a fatal termination usually follows after no long interval. Death may be ushered in with uræmic coma or convulsions, or it may result from syncope or collapse.

Often, however, the attack is by no means so severe in character as would be gathered from the preceding account, especially at the first onset of the malady. It is apt, indeed, to begin with comparatively mild paroxysms, which are practically indistinguishable from those of an ordinary intermittent fever, the distinctive feature of the excretion of hæmoglobin in the urine being altogether absent. These slight attacks—the *petit mal* of hæmoglobinuric fever, so to speak—arise with a feeling of general malaise, accompanied after a day or two, or perhaps after a few hours only, with more or less aching in the head and back and a sense of chilliness, which may rarely increase into a definite rigor.

At this stage there is a slight rise of temperature, the skin is hot and dry, and the eyes are suffused. Loss of appetite is generally experienced, a feeling of nausea also, and occasionally actual vomiting: the mouth feels parched, the tongue is dry and coated, and usually the bowels are confined. Eventually the patient falls into a more or less profuse perspiration, the temperature falls again to normal or thereabouts, the various pains and aches disappear, and the attack appears to be at an end. This may indeed be so; or, on the other hand, it may be followed at intervals of short but varying duration by one or more relapses. At still longer intervals of time the whole series of events may be repeated.

Thus a medical missionary, known to the writer, states that, while working in the Niger district, he suffered from such attacks on an average every month during the first eight months after arriving in Africa; these being followed, at the end of such period the greater portion of which had been actually spent in that country, by a typical attack of "blackwater fever." Three months later, while paying a visit to a large Mohammedan city some distance from the Niger, he suffered from a second attack, of similar character but slighter in its intensity than the former. A voyage to and from England, with a short stay in this country, now intervened, during which stay he had several unexplained attacks of hæmaturia, unaccompanied, however, by fever. A year after the first appearance of the disease in a characteristic form, he suffered from a third attack, which came on about three months after his return to Africa. In this instance a spell of hard work, both mental and physical, added to chronic constipation induced by much travelling in native canoes, seemed to have paved the way for a recrudescence of the malady.

Diagnosis. — Probably the only disease for which hæmoglobinuric fever is likely to be mistaken is yellow fever. The invasion of both diseases is marked by somewhat similar symptoms; but, after the first few hours at any rate, no great difficulty is likely to be found in diagnosing the true nature of the illness.

Hæmoglobinuric fever is endemic, and is not contagious; yellow fever for the most part occurs in epidemic form, and is readily communicable from one person to another. An attack of yellow fever confers immunity from subsequent invasion of the system by that disease; hæmoglobinuric fever may occur many times in the same person. A single attack of hæmoglobinuric fever differs from yellow fever in that its course is irregular in duration and intensity; the febrile paroxysms frequently intermit; the spleen becomes enlarged; the matter vomited consists for the most part of dark-coloured bile (whence the name bilious remittent fever) instead of blood browned or even blackened in the stomach; hæmoglobin, or a derivative of it, and in consequence albumin, is present in large quantities in the urine at an early stage; and, concurrently with this, marked alterations are found in the composition of the blood, as also in the number and shape of its formed elements; intense pigmentation of the skin also appears.

Pathologically the points of difference between these two diseases are even more marked after death from hæmoglobinuric fever. The stomach shows no special alteration, except that its internal surface may appear pale and anæmic; but in yellow fever the mucous membrane is for the most part soft and injected, and the cavity of the organ usually contains blackened and disintegrated blood. In yellow fever the spleen is soft, but not enlarged; the liver is more or less fatty and enlarged, pale in colour, and somewhat soft in consistence. In hæmoglobinuric fever, on the other hand, enlargement of the spleen is often marked, and the liver is hyperæmic and contains an abnormal amount of pigment.

Pathology and Morbid anatomy.—Unfortunately our knowledge of the pathology of this affection is at present somewhat scanty. The most remarkable feature observed in hæmoglobinuric fever is the enormous and often sudden destruction of blood corpuscles in the circulation. The free pigment resulting from such hæmolysis is mainly eliminated by the kidneys, and gives rise to hæmoglobinuria; while a portion is temporarily stored in the liver and other organs, including the skin. When the extent of the hæmolysis is but slight, the liver may be capable of dealing with all the unattached pigment in the blood plasma, in which case hæmoglobinuria is absent. If, on the other hand, the blood destruction be very great and sudden, the kidneys may suffer temporary or even permanent damage from the irritation caused by the passage through them of large quantities of the débris resulting from the extreme hæmolysis.

The exciting causes of a paroxysm have already been discussed; but it is obvious that there must be some previous condition of instability of the corpuscles, as chill, for instance, would of itself be quite incapable of bringing about such a wholesale destruction of the formed elements of the blood. So far as is at present known, the reason for such excessive vulnerability of the formed elements of the blood is to be sought in the continued action of a malarial poison on the system generally, and on the blood vascular system in particular.

The removal of hæmoglobin is not, in the case of every affected corpuscle, the result of the direct action of a parasite; for many of the pallid and deformed corpuscles contain no parasites: it is rather, as Dr. Manson has suggested, the result of some solvent principle in the liquor sanguinis, possibly a digestive agent, which enables the intra-corpuscular parasite to assimilate hæmoglobin, and which, on the breaking up of the sporulating parasite, may be set free in the liquor sanguinis, and continue its solvent action on corpuscles which are not attacked by the parasites themselves. In this way Manson seeks to explain the loss of hæmoglobin seen in all the blood corpuscles in malarial disease, and the acute loss of hæmoglobin in all the corpuscles in hæmoglobinuric fever.

Nevertheless, it is perhaps open to question whether the actual paroxysm which, with its attendant symptoms, presents the characteristic features of an attack of hæmoglobinuric fever, can properly be regarded as but a special phase of the disease strictly known as malaria.

The *blood*, when examined during or immediately after an acute paroxysm, shows under the microscope profound alterations in the consistence, shape, and colour of the corpuscles, the number of which is also greatly diminished. *Rouleaux* formation may be absent altogether, or at any rate extremely imperfect; while poikilocytosis is well marked, different corpuscles being seen to be crescent, spindle, or pear-shaped. Both macrocytes and microcytes will be found, the former being for the most part pale in tint, or even apparently colourless, while the latter are not unfrequently of a deeper hue than normal. Those of the corpuscles which appear to have undergone no appreciable alteration in size, are also for the most part of a paler tint than is usual under ordinary conditions; the contained hæmoglobin having become separated from the stroma and dissolved in the surrounding plasma.

Marked as these appearances are, and great as must be the destruction of corpuscles during the acute phase of the disease, the blood rapidly tends to revert to a more normal state as soon as an attack passes off; the regeneration of corpuscles is indeed so rapid that, unless a further paroxysm intervene, a day or two usually suffices for the poikilocytosis to disappear almost completely: the oligocythæmia is more persistent. If after such an interval a further examination of the blood be made, the corpuscles will now be found to run into rouleaux; there will be less variation in their colour, size, and shape, and both microcytes and macrocytes will have practically disappeared.

Accompanying such regeneration a very definite leucocytosis and an increase in the number of hæmatoblasts are not unfrequently observed.

The *urine* presents characteristics very similar to those met with in the paroxysmal hæmoglobinuria known in this country. It is usually of an acid reaction and of specific gravity above the normal. In colour, that which is first passed during a paroxysm is of a deep reddish or almost black tint, the amount of the contained pigment being large; while when the attack is less severe, or is passing off, it may exhibit all variations of hue between that of port wine and of dark sherry. The total amount of urine passed, at any rate in the first instance, may be small; in this case it is often thick, of a gummy consistence, and contains a large proportion—one-third or even more—of albumin. If the latter substance be precipitated, by means of heat or nitric acid, the coagulum carries down with it the greater portion of the pigment present, leaving the upper stratum of liquid of almost the normal colour of the urine. On standing a considerable precipitate is formed which, when examined by the microscope, is found to consist for the most part of granular débris of a brownish colour, among which larger pieces of black pigment may occur, together with a number, often enormous, of granular hæmoglobin casts, a variable number of hyaline casts, and a few epithelial scales.

Red blood corpuscles are for the most part conspicuous by their absence. In certain instances, however, the hæmoglobinuria is accompanied by a true hæmaturia as well: in some instances this is probably due to the intense irritation of the kidney set up by the elimination of so great a quantity of effete products. When this is the case, blood corpuscles in greater or less numbers will of course be found in the urine.

Dr. Manson discovered certain oval bodies in the urinary sediment, occurring singly or in groups of two, three, or more, the exact nature of which remains undetermined.

Spectroscopically examined in a thin layer, or diluted to the requisite degree, the absorption bands characteristic of hæmoglobin present themselves. Occasionally the presence of a third band, situated between the C and D lines, affords evidence of some of the pigment having become converted into methæmoglobin.

In a communication to the Pathological Society of London Dr. Wheaton describes the appearances met with in microscopic specimens of certain organs obtained from a case of this disease. The kidneys showed in their cortical portions marked swelling of the epithelium and the secreting tubules; the cells were opaque, their outlines were indistinct, and they contained yellow granules: the lumen of the secreting tubules was also packed with small yellow pigment granules. The tubules in the pyramids were filled with large brown amorphous masses of pigment, which were also visible here and there in the form of brown masses within the cells lining them. Beneath the capsule were collections of similar pigment; the Malpighian corpuscles, however, were unaffected. Pigment masses of similar character were also to be found throughout the substance of the spleen, both between and within the cells. The cells of the liver had undergone cloudy swelling and also contained globules of yellow pigment. No blood corpuscles were to be seen extravasated in the tissues anywhere; neither was there blood pigment in the capillaries of any of the organs. It will thus be seen, as Dr. Wheaton suggests, that the pathological appearances of blackwater fever coincide with those which have been found in paroxysmal hæmoglobinuria, so far as can be learned from the records of the latter disease, which are very scanty as it so rarely proves fatal. Clinically, also, these two diseases appear to correspond fairly closely, except that the bilious vomiting and high mortality of blackwater fever are not met with in paroxysmal hæmoglobinuria. The greater severity of the disease as met with in tropical countries is probably due to the greater intensity of the causes.

In addition to these yellow pigment particles in the cells of the various organs, the black pigment, so characteristic of malarial infections, will be found in the usual situations [see art. "Malarial Fever," p. 729].

Treatment.—If it be the fact that blackwater fever is to be regarded as a concomitant of a severe form of malaria, the treatment of the two affections must necessarily be more or less similar. The bowels must be freely opened by drugs—of which calomel and jalap, either separately or combined, are the most generally useful—aided by enemas; and if severe vomiting be present treatment must be especially directed to this symptom. It is recommended to give quinine often and in fairly large doses; though its use would seem to be contra-indicated in the stage of actual pyrexia. Manson, however, appears to consider that this drug is comparatively useless in all cases, and that it exerts no influence in cutting short the duration of an attack; and Plehn, who has had extensive experience of blackwater fever in the Cameroons, believing that it aggravates the tendency to hæmolysis, deprecates altogether the use of quinine in this disease. On the appearance of hæmoglobinuria Plehn discontinues quinine at once, to resume it subsequently when this symptom has subsided, and the fever has returned to the ordinary intermittent course. During hæmoglobinuria he contents himself with a mere treatment of symptoms, and the results he shows are more favourable than are those of physicians who adopt heroic dosing with quinine. If ice can be obtained the patient should be allowed to suck it continually; and small doses of brandy or champagne will probably be retained even when nothing more nutritious can be given by the mouth.

In severe cases it will be necessary to resort to nutrient enemas, and, if the temperature should fall below normal, hot-water bottles may be placed in the bed. Resort may also be had to intravenous injections of normal saline solution, which can be made by dissolving a dram of common salt in a pint of water, boiling the mixture to sterilise it, and then allowing it to cool to a temperature of 105° F. prior to use; experience has shown that better results may be thus obtained than if a lower temperature be employed. In those cases in which nephritis supervenes, there is frequently a tendency to suppression of urine; this indeed, according to Crosse, is an almost constant event in the most serious cases. Such a contingency must be met by the use of diaphoretics; and, if uræmic convulsions or coma supervene, trial should be made of chloral hydrate in conjunction, perhaps, with small doses of jaborandi.

S. Monckton Copeman.

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S. M. C.

AMŒBIC DYSENTERY

SYNONYMS.—*Amœbic enteritis, Tropical dysentery.*

Definition.—A form of intestinal flux caused by a species of amœba; characterised anatomically by ulceration of the large intestine, and clinically by a variable course often marked by periods of intermission and exacerbation; with a special tendency to chronicity and formation of abscess in the liver.

The name "dysentery" was originally a purely clinical one, signifying an intestinal flux, the symptoms of which are abdominal pain, tenesmus and the passage of bloody mucoid evacuations. Attempts have subsequently been made to connect the above symptoms with definite lesions of the intestinal tract; but inasmuch as these lesions are found to vary considerably in individual cases, or in series of cases, there arose much confusion in the classification of dysentery, as is well illustrated by the long controversies between the German and the French schools of pathological anatomy. The former, from a study of the sporadic or epidemic dysentery of their own country, maintained the association of diphtheritic inflammation with the intestinal lesions; the latter, on the basis of a study of dysentery in tropical or subtropical colonies, as stoutly denied it.

Recently the attention of investigators has been drawn more particularly to the ætiological factors concerned in the production of dysentery; with the result that a provisional basis for the classification of dysentery has become possible: for one of its forms, at least, a causal agent has been found which, although not fulfilling entirely the conditions required for absolute proof, is nevertheless to be considered as the most probable ætiological factor in a certain important group of cases.

Two other forms of dysentery have been recognised, namely, diphtheritic dysentery, which constitutes the greater part, at least, of the widespread and fatal epidemics of dysentery in temperate climates, and the so-called catarrhal dysentery which is apt to prevail in the same latitudes at certain seasons of the year, particularly in the autumn. In neither of these clinical forms of dysentery has a constant and specific ætiological factor been demonstrated, though it is highly probable that the former is due to the action of one or more of the schizomycetes.

The name amœbic enteritis, which has been proposed for the disease now before us, obviates the confusion arising from the application of the word dysentery to diseases which have no ætiological connection one with another: but, if it be borne in mind that the word dysentery is used in a purely clinical sense, there can be no serious objection to retaining the older and more familiar term. "Tropical" dysentery can only be used as a partial synonym for amœbic dysentery: for on the one hand the disease, though more frequent in tropical regions, is by no means limited to them; and on the other hand there are undoubtedly cases of dysentery in the tropics which are not of amœbic origin. [*Vide* art. "Dysentery."]

Ætiology.—1. *The Amœba.*—In 1875 Lösch of St. Petersburg gave the first accurate description of an amœboid organism which he found in the stools of a dysenteric patient, and to it he gave the name *amœba coli*. He asserted that this organism is the cause of dysentery; and he succeeded in producing a superficial ulceration of the large intestine in one of four dogs which had received rectal injections of the dysenteric stools. Lösch's observation has been confirmed by various researches in different countries: namely, in Europe by Hlava, Kartulis, Kovacs, Quincke, and Manson; in Africa (Egypt) by Koch, Kartulis, Kruse and Pasquale; in North America by Osler, Councilman and Lafleur, Musser, Dock, and others; in Brazil by Lutz. The interpretation of these observations, however, has given rise to much discussion; some observers maintain that the amœba is a harmless parasite of the normal intestine, others that it is the cause of a special form of dysentery.

(*a*) *Morphology, and physical and biological characters.*—This organism is placed by Leuckart in the class Rhizopoda of the Protozoa; by Grassi in the class Lobosa, which includes only a part of the Rhizopoda. It is a unicellular organism consisting of slightly differentiated masses of protoplasm, and under favourable circumstances it exhibits spontaneous movements.

In a state of rest the amœba assumes a spherical shape, which appears discoid in the field of the microscope. It may generally be distinguished from the other cellular elements found in the fæces by its pale greenish tint, and by its stronger refraction of light. Its diameter varies within wide limits, 6 to 35 μ, more commonly between 12 and 26 μ. It is noteworthy that such differences in size are found, as a rule, in different cases of the disease, while the amœbæ in any individual case are nearly uniform in diameter. The body of a resting amœba has a well-defined regular border, which under ordinary conditions appears as a thin, single, dark line. The body consists of two portions: the inner one, which is more or less granular and of a darker colour, is known as the entoplasma; the outer one, which is homogeneous and of a lighter colour, as the ectoplasma.

This division into two zones cannot always be made out, and is more evident in the motile than in the resting amœba; indeed Kruse and Pasquale affirm that it does not exist in the latter.

The *entoplasma* varies more in its appearance than does the ectoplasma. It constitutes the greater portion of the body of the amœba, being usually centrally situated, but occasionally slightly eccentric. In the smaller forms of amœba it is finely granular, and may show no other structure. In the larger forms it is more coarsely granular, and often contains clear, circular or slightly oval spaces—known as vacuoles. These are extremely variable in number and size; some amœbæ contain a few only, while others appear to consist of a congeries of vacuoles surrounded by a very narrow zone of clear ectoplasm.

The *ectoplasm* is quite homogeneous, forming a zone of variable thickness around the entoplasm. It has the appearance of finely-ground glass of a distinctly pale green tint.

In most amœbæ a nucleus can be seen. Its detection is by no means easy in the motile amœba; but under certain conditions in the motionless or dead amœba the nucleus becomes evident, and it may always be shown by appropriate staining reagents. It is situated eccentrically, at the edge of the entoplasm, and appears as a discoid body about 6 μ in diameter, with a sharp contour which, though occasionally broken and irregular, is generally even; it may be distinguished from vacuoles of the same size by its higher refracting power. A nucleolus can seldom be observed, and in stained specimens only.

Minuter details of structure may be brought out by hardening and staining the amœba in suitable media. Portions of the dysenteric stools richly laden with amœba may be hardened in bulk in Müller's fluid, and subsequently cut and stained like sections of tissues; or a thin layer of the same stools may be spread upon cover-glasses, immersed in the hardening media, and then stained. Better results, however, are obtained by the study of amœba in sections of the tissues hardened in alcohol, Müller's fluid, or Fleming's solution.

In specimens hardened in alcohol and stained with methylene blue—which is on the whole the best method of preparation—the amœbæ are not stained quite so intensely as the nuclei of the tissues; one portion of the body is deeply stained (the entoplasm), but the colour fades gradually into an almost unstained portion. Deeply-stained round granules of different sizes are seen scattered throughout the cell body. In specimens hardened in Müller's fluid and stained with hæmatoxylin and eosin, there is less shrinkage than with other media; and the nucleus is clearly visible. Specimens hardened in Fleming's solution and stained with safranin and acid fuchsin give the best picture of the nucleus; and in some of them the amœbæ exhibit other peculiar structures. Among these may be noted short, rod-like bodies resembling tubercle bacilli; they correspond to similar bodies found in the surrounding tissues, and are probably nuclear detritus. Again, in specimens treated in the same manner, somewhat longer rods have been observed radiating from the periphery of the nucleus towards the circumference of the amœba. Their significance is not known.

It is to be observed that, whatever the method of preparation, the nucleus stains with difficulty; a feature common to all the Protozoa. Foreign bodies are frequently seen in the amœbæ, especially red blood cells. These are sometimes so numerous that the whole body of the amœba is filled with them; they may be in a perfect state of preservation, or quite decolorised and only recognisable by their outline: they are certainly more numerous in the more acute cases, or in exacerbations of chronic cases of dysentery.

The amœba rarely contains leucocytes, and never fat globules. Micrococci, bacilli, and their spores are more or less frequent inclusions.

Black pigment granules and irregular brownish masses of pigment have been noted by some observers; it is probable that these are derived from disintegrated red blood cells.

The most striking and characteristic feature of the amœba is its mobility. This may consist either in an alteration of its shape or in an actual change of place. Both of these phenomena are produced through the mechanism of pseudopodia. These latter are rounded, blunt and homogeneous processes formed by the more or less gradual protrusion of a portion of the ectoplasm at some part of the periphery of the amœba. The motion is sometimes quite gradual and continuous, at others sudden and jerky; and it varies in rapidity under circumstances which will be described further on. It is sometimes so rapid that it becomes impossible to make a sketch of the form of the amœba at any given moment; while again the movements may be so slow and deliberate that prolonged observation is necessary to detect any change of shape. Frequently the pseudopodia are withdrawn in the same manner and protruded at another part of the periphery: quite exceptionally long processes are projected which bend around and form an elbow, so that the blunt point of the pseudopodium becomes connected with the amœba at some other point. In other instances a protuberance of the ectoplasm appears to course, as a protoplasmic wave, around the circumference of the amœba; this effect is produced by the successive projection and retraction of contiguous portions of the ectoplasm.

The progressive movement—that is, actual locomotion—is brought about by the protrusion of pseudopodia in the manner described; and into these, when they have reached a certain size, the granular or vacuolated entoplasm, with its other contents, flows with a more rapid movement than that by which the pseudopodia themselves were formed. When the amœbæ are very active, as on the warmed stage of a microscope, these two stages in the process of locomotion are not to be distinguished; but the amœba changes its place by a rapid rolling or flowing motion, in which no distinction between ectoplasm and entoplasm can be observed. Locomotion is generally observed to take place in the direction of least resistance; a group of cellular elements or some detritus being sufficient to divert the course of the amœba. The amœboid movements are also influenced by various external factors, particularly by variations of temperature. They are most active at the mean temperature of the human body, and become less active at lower as the temperature rises above this mean or falls below it.

As a rule the amœba becomes motionless in a temperature lower than 75° F., but may again become motile if the temperature be raised to body heat; providing that it has not been exposed to the lower temperature for more than a few hours. At the end of twenty-four hours, that is, when the stools become temporarily acid, not only is no movement to be observed, even under the most favourable conditions of temperature, but generally every trace of amœba has disappeared.

Sulphate of quinine (in a solution of $\frac{1}{5000}$) arrests the amœboid movements instantly; the organisms assume a circular outline, and their contents become pale and blurred. With various colouring solutions, such as carmine or methylene blue, the peculiar motion in the form of protoplasmic waves noted above occurs; but the amœba does not take the stain until the movements cease, presumably on the death of the organism. Foreign bodies in the amœba are stained, and finally the amœba itself. After certain kinds of local treatment, as by irrigations of the bowel with various germicidal solutions, the amœbæ in the stools passed with the injections, or immediately after them, are quite motionless.

Kruse and Pasquale describe three forms of degeneration which precede the actual destruction of the amœba; namely, a colloid and a dropsical degeneration, and a dissolution by separation of bud-like fragments of the body. In the first case the amœba becomes homogeneous, and at the same time refracts light more strongly, like a fat globule; in the second the vacuoles swell and burst, and the residual body forms a granular mass; in the last case small roundish portions of the amœba are gradually detached from the parent mass, somewhat like the budding of the yeast fungus. That this is not a form of reproduction is signified by the still undivided and unaltered nucleus.

Practically nothing is known of the conditions of nutrition, respiration, and reproduction of the amœba. The frequency with which red blood corpuscles are found in actively moving amœbæ, sometimes in considerable numbers, suggests that these are taken up as food stuffs by a process of inclusion; this, however, has never been actually observed. The pigment contained in some of them is the only evidence of the destruction and assimilation of the blood-cells; and no observation is recorded of the ejection of residual and excrementitious matter from the body of the organism. The vacuoles appear to play no part in the digestive processes of this species. It is probable that a portion of the food of the amœba is obtained by the process of diffusion. It is difficult to understand how respiration and oxidation processes are carried on by it in fluids poor in acids such as those in which the organism lives. It might indeed be supposed that their oxygen was derived from the absorbed red corpuscles, were it not probable that a reduction of their hæmoglobin had already taken place in the intestinal contents, which are rich in carbon dioxide (Kruse and Pasquale). No observations are even recorded of reproductive processes in the amœba. Analogy would lead one to assume, however, that this takes place by fission or by sporulation; that the former may be the usual method is suggested by the fact that small forms of amœba, such as one would expect to find in case of spore formation, are very seldom found in the stools. As an indication of commencing fission may be instanced the occurrence of a slight hour-glass constriction of the body joined by a faint line which possibly represents the formation of a cell-membrane between the two segments.

Resistant forms of the amœba, the so-called "encysted amœbæ," have been noted, after calomel had been given, by Cunningham, by Grassi and Calandruccio, and by Quincke; but by no later observers. That such forms occur, and are necessary, under some circumstances, for the transmission of the disease from one person to another, may be inferred from an experiment by Kruse and Pasquale, in which dysenteric stools rich in active amœbæ, after thorough freezing and subsequent thawing, were still capable of producing an amœbic enteritis in cats; though the organisms could not be detected in the stools thus treated. A similar experiment with stools which had never contained amœba was negative in its results.

(*b*) *Occurrence of amœba in dysenteric stools.*—Amœbæ were found in the stools by Kruse and Pasquale in forty out of fifty cases of the disease; by Kartulis in every case in nearly 500 observations; and by Councilman and Lafleur in thirteen out of fifteen cases, while in their remaining two cases the amœba was found post-mortem, either in the material scraped from the base of the intestinal ulcers or in sections of the latter. The number found is very variable. In some cases actively moving amœbæ are found in great numbers in every stool examined throughout the course of the illness; while in other cases they can be detected only on a long and careful search. As a general rule they are more numerous and more frequently present in the acuter cases and in the earlier stages of the disease, or in the periods of exacerbation of chronic dysentery; and they disappear more or less gradually from the stools during convalescence.

Occasionally the intestinal ulceration is latent, the motions being quite formed with but small flakes of mucus adherent to them, in which no amœbæ may be found; in these cases the existence of dysentery is not suspected until an abscess of the liver occurs in which actively motile amœbæ are found, either by exploratory puncture, or in the sputa if the abscess evacuate itself spontaneously through the bronchi. Failure to detect amœba in the stools is frequently due to delay in the examination of them: as noted above, the organisms very often disappear from the stools in a few hours. After intestinal irrigations of astringent or germicidal substances the organisms are always diminished in numbers, and may even disappear altogether from the stools for many days.

(*c*) *Occurrence of amœba in the stools of persons who are in good health, or are suffering from diseases other than dysentery.*—Numerous investigations have demonstrated conclusively that amœbæ may be present in the fæces of healthy persons. Such cases are reported by Cunningham, Grassi, Schuberg, Kruse and Pasquale. They have also been found in cases of chronic diarrhœa, cholera, intestinal tuberculosis, typhoid fever, hæmorrhoids, and other diseases; chiefly in such as are accompanied by looseness of the bowels. It may be remarked that not a few of the cases cited as chronic enteritis, or chronic diarrhœa, were in all probability examples of the more chronic form of amœbic dysentery; but it is impossible to apply this statement to all cases.

Temporary looseness of the bowels in otherwise healthy persons, either as the result of slight indisposition or of medication, seems to be a condition of the presence of amœbæ in the stools. Schuberg found these organisms in ten out of twenty loose stools produced by the administration of Carlsbad salts. He concludes that the amœba is a normal and harmless parasite of the cæcum and ascending colon; and that the reason for its non-appearance in ordinary fæcal evacuations is the solidity and acid reaction of the contents of the lower bowel, which soon destroy it.

The question naturally arises whether more than one species of amœba is found in the human intestinal tract? So far no definite morphological differences have been found between the amœba occurring in the stools of healthy persons and that in patients suffering from dysentery. A certain difference, which has been proved as regards inoculation experiments, will be described further on.

(*d*) *Culture experiments.* — No deductions can be drawn from the earliest attempts to cultivate the amœba; namely, those undertaken by Cunningham in 1881. This was before the days of careful bacteriological technique; and the experiments are open to criticism, inasmuch as the culture fluids—the alkaline fluid of cholera excreta and the solutions of cow-dung—used by this investigator were not proved before use to be sterile. To the more recent experiments of Kartulis, in which straw-infusion was the medium employed, objections as serious may be raised; for, though the fluid media were sterilised, the only flasks in which a growth was observed were those which had been left unstopped, and were thus open to aerial contamination. Indeed, with Schuberg and Kruse and Pasquale, it may be asserted that the "spore-forms" and "amœba-swarms" described were nothing else than straw-infusion amœbæ (*Strohamöben*).

Culture experiments with fluid blood serum and fluid gelatine were not successful. It may, then, be stated definitely that no one yet has succeeded in producing pure cultures of amœba.[1]

(*e*) *Inoculation experiments.* — It is evident that, in the absence of artificially produced pure cultures of amœba, such experiments must have been undertaken with impure (that is, mixed) cultures; in other words, with material such as dysenteric stools or the contents of hepatic abscesses. In a few cases, however, it has happened that cultures accidentally pure have been made use of, as in the case of material from an hepatic abscess which was found to contain no organisms other than amœba. It is obvious that the deductions drawn from the latter experiments may be considered as trustworthy as if drawn from experiments with pure cultures artificially produced; but no such certainty can be ascribed to the experiments first mentioned.

The animals experimented upon have been cats, dogs, monkeys, hens, guinea-pigs, and jerboas; of these, cats have been found the most susceptible.

Inoculations may be made in three ways: by feeding animals with material containing the amœba; by inoculations of the small intestine after a preliminary laparotomy; and, finally, by rectal injections with or without suture of the anal orifice. The first method has always proved unsuccessful except when encysted forms were present (Quincke and Roos); probably because of the destructive action of the gastric juice on the amœba. To the second method the objection has been raised that the manipulation of the intestines and the use of antiseptic solutions during the course of the operation are in themselves a source of irritation to the bowel, and in some cases have produced an enteritis. The third method is the simplest, and has given positive results in the hands of Lösch, Hlava, Kartulis, Kovacs, Quincke and Roos, and Kruse and Pasquale.

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[1] Celli and Fiocca appear to have recently succeeded in obtaining pure cultures of amœbæ. They describe a life-cycle in two phases—the amœba form and the cyst form. The amœbæ multiply by division. (*Centralblatt f. Bakt.* v. 15.)

The results of the last two observers are deserving of special mention. Dysenteric stools, or material from hepatic abscesses containing amœba, were injected into the rectum of various animals, with or without subsequent closure of the anus, for twenty-four or forty-eight hours. In some cases, chiefly those in which motionless amœbæ were injected, no abnormal result followed; in others blood-tinged mucus, containing actively moving amœbæ, appeared in the evacuations from the second day or thereabouts, but the animals did not appear to be ill; in a third series, with evacuations of a like character, the animals wasted and died after a variable number of days. In both the second and third series of cases post-mortem examination showed pathological changes in the large intestine, proportionate, as a rule, to the severity of the symptoms. To this series of experiments belongs the one previously recorded, in which stools rich in active amœbæ were thoroughly frozen, then thawed out and injected into the rectum of a cat in the usual way. In this case, notwithstanding the complete disappearance of the amœbæ in the thawed stools, the injection was followed by a definite experimental dysentery in the animal; presumably as the result of the development of the so-called "encysted" or resistant forms of the organism. Of especial interest also are the experiments made with material from liver abscesses which was proved to contain no other organism than the amœba. Three such cases are recorded in cats, in all of which an experimental dysentery was produced.

The severity of the experimental disease thus produced is directly as the numbers and activity of the amœbæ injected, and inversely as the age of the animal experimented upon.

The lesions found are reddening and swelling of the intestinal mucosa, chiefly of the lower half of the large bowel, with here and there ecchymoses, small superficial areas of necrosis, and shallow ulcerations. The mesenteric glands and the solitary lymphoid follicles are often swollen. In the blood-tinged mucus covering the mucous membrane amœbæ are found in greater or lesser numbers. Microscopical examination of sections of the intestine shows that the necrosis is limited, as a rule, to the mucosa; and that beneath it the submucosa is thickened and œdematous, and its vessels engorged; there is also some small-celled infiltration. Amœbæ are found in the borders of the ulcers, chiefly in the

Lieberkühnian follicles; in the base of the ulcers they rarely penetrate more deeply than the upper layers of the submucosa. With the amœba are found many bacteria, chiefly streptococci.

From a comparison with the lesions of amœbic dysentery in man it will be seen that while the processes in man and in the cat are not absolutely identical, more especially as regards the depth and extent of the ulceration, yet in many points the resemblance is striking.

A series of control experiments was undertaken, by the authors quoted, with amœba from the stools of healthy individuals and with the straw-infusion amœbaof Kartulis. In neither of these cases could an experimental dysentery be produced in any of the animals inoculated. They conclude that it is proper to designate the pathogenetic amœba as the *amœba dysenteriæ* (Councilman and Lafleur), and to retain the name of *amœba coli* (Lösch) for the non-pathogenetic amœba of the normal healthy intestine. The experiments with pure cultures of bacteria isolated from the dysenteric stools and hepatic abscesses will be referred to in Section 2.

(*f*) Concerning *the source of the amœba* and the mode of infection little can be positively stated. On the one hand the life history of the amœba outside of the human body is not known, all attempts at cultivation having failed; and, on the other, inoculation experiments by way of the mouth, with the exception of those undertaken by Quincke and Roos with the so-called encysted forms, have been uniformly unsuccessful. It is reasonable to suppose, however, that this must be the usual path of infection, and that the amœba in all probability is taken with drinking-water. In one case investigated by myself the water-supply was examined, but no organisms resembling the amœba were found in it.

2. *Other organisms found in amœbic dysentery.*—In the dysenteric stools a great number of bacteria of various species and some flagellated infusorial organisms are associated with the amœba. Among the latter are the *cercomonas intestinalis* (*megastoma entericum*, Grassi), the *trichomonas intestinalis*, and more rarely the *balantidium coli*. The first-mentioned organism consists of a clear, bladder-like body, tapering at one end, which is provided with delicate flagella, usually four to six in number, by means of which the parasite moves rapidly from place to place with a wavy motion. Viewed in profile it is somewhat sickle-shaped. The *trichomonas* is distinguished from the *cercomonas* by having more flagella, and on one side a narrow undulating membrane.

These bodies are found in diarrhœal evacuations, never in the solid fæces; and as frequently without amœba as in association with it. They do not appear to have any pathological significance, but it is possible that they may keep up diarrhœal discharges.

Of the bacteria many are normal inhabitants of the intestinal tract, while others appear only in pathological states of the intestinal walls.

The earlier investigations were made in cases of diphtheritic dysentery, sporadic or epidemic, occurring in temperate climates; and no association with amœbæ was noted. Inoculation experiments resulted, in some of these cases, in the production of an experimental diphtheritic dysentery.

The cases in which impure cultures were used may be dismissed without further consideration. Chantemesse and Widal, however, succeeded in producing ulceration of the intestine in guinea-pigs, by inoculations, by way of the mouth or by the intestine after laparotomy, with pure cultures of a short slightly motile bacillus obtained from five cases of tropical diarrhœa; and Ogata has attained the same result during an epidemic of dysentery in Japan.

Of more interest are the observations of Kruse and Pasquale on the bacteria found in association with amœba in dysentery; for in this case it is possible to compare the pathogenetic properties of the latter with those of the former; as well as their distribution in the affected tissues. In 100 cultures from fresh dysenteric stools and the contents of liver abscesses, and (post-mortem) from several organs, there were found streptococci of various species in 50 per cent; typhoid-like bacilli in 25 per cent; the bacillus pyocyaneus, a bacillus resembling the pseudo-diphtheritic bacillus, and the staphylococcus pyogenes. None of these organisms was present so constantly, or in such numbers, as to suggest a specific relation to the dysenteric lesions. Post-mortem the associated bacteria were always most numerous in the blood from the portal vein; which seemed to point to direct absorption from solutions of continuity in the intestinal mucous membrane.

Inoculation experiments on cats, conducted in the same manner as those previously referred to, gave a negative result. It must not, however, be concluded from this that the bacteria found in association with the amœba possess no pathogenetic properties whatever, but rather that they cannot be regarded as the primary agents in this form of dysentery. Certain details in the pathological anatomy of amœbic dysentery can scarcely be explained without the co-operation of associated bacteria —notably such as may be concerned in diphtheritic inflammation.

3. *General ætiological factors.*—*Geographical distribution.*—Amœbic dysentery occurs in tropical, subtropical, and temperate climates; but from the observations of Kartulis it must be concluded that it is endemic and more prevalent in the warmer regions of the globe; if indeed it be not the usual form of dysentery in those latitudes. In illustration of the frequency of its occurrence may be mentioned the following localities:— in North America: sporadic cases in the New England States; a more considerable number in Maryland and the adjoining States, and in the Mississippi Valley; and a series of cases in Texas, on the shores of the Gulf of Mexico. In the Eastern Hemisphere: sporadic cases in Germany, Austria, and Italy; endemic foci in Greece; and a large series of cases in Egypt (where the disease has been more particularly studied). No observations have as yet been made in India, Southern China, or the East Indies. It is very desirable that the frequent cases of dysentery in tropical countries should be investigated with reference to the occurrence of amœba; in this way alone can it be determined whether the prevailing form of dysentery, which from the clinical and anatomical descriptions of the earlier authors corresponds closely with amœbic dysentery as observed

in the above-mentioned countries, is of identical causation. Such an investigation would be particularly useful in determining the proportion of epidemic dysentery in the tropics which is of amœbic origin; for it is well established that the epidemics of dysentery in temperate climates, such as those occurring in prisons, asylums, military camps, or wherever there are aggregations of individuals under bad hygienic conditions, are not to be classed under this heading. Amœbic dysentery in temperate climates shows no tendency to become epidemic, even when there are endemic foci; and no example of contagion direct or mediate has been adduced.

Meteorological conditions appear to have considerable influence on the incidence of the disease. In Baltimore, out of thirteen cases in which the date of the onset of the illness was known, twelve occurred between the months of April and September; that is, during the warm season.

No observations have been made on the effect of conditions of soil, of elevation, or of relative humidity. In North America, however, the disease has been observed most frequently in districts approaching the sea-level; namely, the shores of the Chesapeake Bay and the Gulf of Mexico, and the Mississippi Valley. It occurs in the dry climate of Egypt, and on the Atlantic sea-shore where the relative humidity is high.

The influence of water-supply for drinking purposes on the development of amœbic dysentery is unknown; though it seems likely that this may be a frequent if not the principal source of infection.

Overcrowding, insufficient or unwholesome food, antecedent illness or debility do not appear to enter into the causation. In a few recorded cases there was an intermittent and mostly painless diarrhœa preceding the more or less acute onset of dysenteric symptoms; but it cannot be affirmed that the dysenteric process was not actually in existence, for such diarrhœas, with amœba in the stools, constitute one of the modes of onset of the disease; and are, moreover, frequently observed between the periods of exacerbation in subacute or chronic cases. Sex, age, and occupation do not appear to be important ætiological factors. From the observations of Kruse and Pasquale it would appear that in Egypt, at any rate, recently immigrated foreigners are more frequently attacked than natives.

Pathological anatomy.—The intestinal lesions are found in the large bowel; very seldom is the portion of the ileum immediately adjoining the ileo-cæcal valve affected. The extent to which the intestine is involved varies very much: in some cases there are numerous and uniformly distributed lesions from the cæcum to the rectum; in others some segments of the bowel suffer severely, while the rest escapes without any obvious reason for such immunity. In the majority of the cases the cæcum and ascending colon are affected.

The pathological changes consist in a thickening of the bowel, followed by necrosis and the formation of more or less extensive and deeply-excavated ulcerations. Thickening of the bowel is a constant and very characteristic anatomical feature of this form of dysentery. It may involve all the intestinal tunics; but it is specially marked in the submucosa, and sometimes limited to it: it consists in a general œdema and in localised areas of thickening. These latter appear on the surface of the mucous membrane, particularly on the summit of its folds, as sharply-circumscribed hemispherical or ovoid projections over which the membrane is slightly reddened or discoloured; when incised they are found to contain a pale or grayish yellow viscid material.

In a later stage a portion of the mucous membrane over these elevations becomes œdematous and necrotic, and is then cast off, leaving a small opening through which may be seen the semi-fluid necrotic material in the submucosa. The ulcer thus formed tends to spread by further implication of the submucous coat, followed by further destruction of the overlying mucous membrane.

In the same case every gradation may be observed between the nodular thickenings and the extensive ulcerations of the bowel. When the ulcers are adjacent they are frequently connected by sinuses in the submucous coat which contain the same viscid material as the cavity of the ulcers, and are bridged over by the still intact mucous membrane. On microscopical examination this viscid material is found to consist of a granular detritus, elastic tissue fibres, red blood corpuscles, pus cells, large round swollen uninuclear cells (which sometimes contain fat drops, probably altered connective tissue corpuscles), and amœbæ more or less abundant. If the autopsy has been held within a few hours after death some of the amœbæ may be observed in motion. The most characteristic ulcers have soft, ragged, deeply-undermined borders, somewhat raised above the level of the surrounding mucous membrane owing to the infiltration of the subjacent submucosa. The base is formed by remnants of the submucous tissue adhering in the form of shreddy sloughs; in the older ulcers it is a clean smooth granulating surface, with a marked absence of purulent material.

The muscular coat offers a great resistance to the extension of the process; and in those cases in which there is deeper ulceration, the advance is made along the intermuscular septa to the subperitoneal connective tissue, which then becomes œdematous and necrotic in the same way as the submucosa. In this manner more or less extensive areas of the muscular coat are dissected out and cast off, as was the mucous membrane by the extension of the process in the submucosa.

This progressive implication of the connective tissue layers of the intestine is one of the most characteristic features in the anatomical lesions of amœbic dysentery—especially in very acute cases, where sloughs several inches in length may be recognised in the stools; these on microscopical examination are found to contain the elements of the mucosa or of the muscular coat of the bowel. When the subserous connective tissue has been infiltrated the peritoneum becomes greatly thickened, and adhesions form between adjacent loops of intestine, or between the bowel and neighbouring organs, which may result in kinking or distortion of the bowel.

Besides this ordinary form there are ulcers with but slight undermining of their edges; others with smooth borders and clean bases, where the disease is not advancing; and yet others in which there is a marked purulent infiltration. These varieties are produced by varying conditions in the rapidity of the process, in the layers of tissue engaged, and, especially, by the association of other organisms with the amœba.

The mucous membrane is, as a rule, affected secondarily; but occasionally there are small superficial necroses at a distance from the ulcers.

The bowel in its diseased portions varies in colour from a deep bluish red, in acute cases, to a slaty gray in the more chronic. In all cases there is an excess of mucus, which is often blood-stained, and forms a considerable part of the dysenteric evacuations. In the experimental dysentery of cats this catarrhal inflammation of the mucosa appears to play a larger part than it does in human dysentery.

Sections of the intestine which include an ulcer and the adjacent healthy portions afford additional details of the pathological process, and show the relation of the amœba and of other micro-organisms to the lesions. In the vicinity of an ulcer the submucosa is swollen to two or three times its normal thickness by the œdema of its fibres and cellular elements; its interstices are much widened; its vascular and lymph channels are engorged; the fixed cells with their nuclei are swollen, and often show fatty degeneration; and the intercellular tissue has lost its fibrillation. There is more or less small-celled infiltration, either in groups or rows or scattered throughout the œdematous tissue; the cells being chiefly of the mononuclear variety (lymphocytes). Much less frequently there are aggregations of pus cells; indeed, the special feature of the infiltration lies in the marked absence of the products of purulent inflammation. There are only slight changes in the overlying mucous membrane, and these consist chiefly in superficial erosions, of cystic dilatations of some of the deeper glands, increase in the mucoid secretion, and some proliferation of the lining epithelium. This zone merges gradually into the zone of necrosis, that of the ulcer properly speaking. Here in the submucosa there is a general liquefaction of the elements of the tissue; the cells lose their nuclei and their power of absorbing staining reagents, while the intercellular substance is changed into an amorphous granular mass. The resistant elastic tissue fibres may still be distinguished among the disintegrated elements. A peculiar hyaline reticulum, which is not fibrin, is sometimes found in the upper part of the necrotic zone. The mucous membrane overhanging the ulcer cavity is œdematous; the epithelium is often shed, or lies loose in the lumen of the gland, and the interglandular substance is softened and infiltrated with pus or granulation cells. Frequently the mucous membrane is folded inwards, forming a covering for the roof and part of the lateral walls of an excavated ulcer; and this may be combined with an actual proliferation of the glandular epithelium, which forms bud-like projections into the underlying tissues. When the ulceration extends to the muscular coat, and beyond it, the superficial muscle fibres are swollen and converted into a homogeneous hyaline material; the intermuscular septa are widened and show a small-celled infiltration. The changes in the subserous layer of the intestine, when this is attacked, are similar to those seen in the submucosa. Fibrinous exudation is seldom found except in the lymphatics and where there are amœbæ.

The amœba is constantly present in the ulcers. The organisms are most abundant in the submucosa; but they may be found in the deeper layers of the intestine when the infiltration extends to the muscular coat and beyond it. In the mucous membrane itself they are seldom found, and then chiefly in its lower portion, where they occupy the interglandular spaces, or lie in the meshes of the muscularis mucosæ. This distribution suggests the idea that they have wandered into the mucous membrane from below, and not from the surface of the bowel. It is exceptional to find them superficially in the rare cyst-like dilatations of the glands. In the submucosa they are present in the greatest numbers in the zone immediately bordering on the central necrotic portion of the ulcer; that is, in the zone of œdema and small-celled infiltration. They usually lie in the lymph spaces, and are surrounded by a clear space; which is probably the result of the unequal shrinkage of the amœbæ and of the tissues under the influence of the hardening agents used in the preparation of the specimen. The lymphatics and, more rarely, the veins also contain the amœba. In the fully necrotic portions of the submucosa the amœba is scarce. Large swollen connective tissue cells in the submucosa often resemble the amœbæ very closely; but in most cases they may be distinguished from the latter without difficulty.

In the muscular coat the amœbæ occupy exclusively the intermuscular septa of connective tissue; especially those which run perpendicularly to the surface of the bowel, and which are, as noted before, much thickened and infiltrated. In this tissue they often lie in rows reaching to the subserous connective tissue. In the loose meshes of the latter they are more scattered, and they may even invade the fat of the mesocolon. Wherever the amœbæ are found the same changes are always to be observed in the tissues; namely, œdema and infiltration with small round cells, and in the rear of the amœbæ, so to speak, necrosis and liquefaction of the tissues.

The number of amœbæ found in different cases, or in the several ulcers of the same case, is subject to wide variations, and depends to a large extent upon the state of preservation of the tissues; thus they are more likely to be found in considerable numbers if specimens for examination have been obtained before marked cadaveric changes have occurred in the tissues. Another important cause of this variation lies in the association of bacteria with the amœba in the intestinal lesions. It is probable that this association exists in every case: but in many instances the lesions are not those which bacteria, particularly the pus organisms, usually produce; and it seems quite justifiable in such cases to attribute the lesions primarily to the action of the amœba. It is quite certain, at least, that bacteria are most numerous in the ulcers that are characterised by purulent infiltration, and are found but sparingly in those in which œdema and small round-celled infiltration are found; and that the reverse is true of the amœba. The bacteria are always most abundant in the upper strata of the necrotic zone of the ulcer, which indeed may be composed almost entirely of them; but they may be found in the neighbourhood of amœbæ that have wandered far into the tissues, and even within the amœbæ themselves. The species found are those already mentioned as occurring in the stools; namely, streptococci, typhoid-like bacilli, and a bacillus resembling the pseudo-diphtheritic bacillus; sometimes one species predominating, sometimes another. Whatever part these organisms play in the genesis of the primary lesions, it is unquestionable that they are responsible for some of the subsequent destructive processes; notably for the disintegration of the mucous membrane over excavated and undermined ulcers in the submucosa.

How the amœbæ establish the foci of necrosis and ulceration is not very clear. It seems probable that they penetrate the mucous membrane by way of the interglandular substance, and so reach the submucosa which is the seat of the primary lesion. The small glandular cysts containing the amœba appear to be so rare that they cannot be taken as the usual initial points of the lesions.

Certain complications of the ordinary dysenteric process remain to be mentioned. Of these the most important is abscess of the liver, which will be found described in detail in another portion of this work (*vide* Amœbic Abscess of the Liver). Diphtheritic inflammation, analogous to the primary diphtheritic enteritis, if not identical with it, is occasionally met with. This is signified by a more or less widespread croupous exudate over the surface of the mucous membrane, with superficial loss of substance; and on histological examination by necrosis of the glandular epithelium, with nuclear fragmentation and extensive bacterial invasion. In these cases it is often difficult to find amœba either in the stools or in the sections of the ulcers.

Small hæmorrhages in the vicinity of the ulcers are not infrequent; more rarely there are large extravasations in the submucosa.

Massive gangrene sometimes occurs, masking the original dysenteric lesions. Undoubted tuberculous ulcers may coexist with dysenteric ulceration. Localised peritonitis, with the production of local adhesions, is frequently met with as the result of the extension of the ulceration to the serous coat of the bowel.

Occasionally the visceral peritoneum becomes folded upon itself, the two contiguous surfaces become adherent, and a kink in the bowel results, which appears on the inside as a boss or ring-like protrusion of the mucous membrane. This is one of the causes of stenosis of the bowel after dysentery. General peritonitis is due in most cases to perforation through the base of an ulcer; it is not uncommon, especially in acute cases accompanied by extensive sloughing of the bowel, and it does not differ anatomically from perforative peritonitis in general. There may, however, be general peritonitis without any perforation. In one such recorded case the whole surface of the peritoneum was cloudy and roughened; and in places was covered with an opaque and gelatinous fibrinous exudate which could be removed with ease and was found to contain the amœba.

The solitary lymphoid follicles are not affected in this form of dysentery; unless they lie close to an ulcer, in which case they are somewhat swollen and surrounded by cellular infiltration. When a diphtheritic enteritis complicates the lesions of amœbic dysentery the changes in the follicles are more marked.

Healing of the dysenteric ulcer is brought about by the growth of granulation tissue from the base and sides of the ulcer, and by the gradual investment of its surface by epithelial growth from the adjoining healthy mucous membrane. It is probable that the peculiar epithelial formations mentioned in the description of the ulcers are in reality the earliest steps in the process of regeneration.

Atrophy of the secretory glands and polypoid outgrowths from the mucous membrane are sequels of the ulceration, but it is remarkable how seldom stricture of the bowel occurs.

Symptomatology.—I. *General characteristics; mode of onset, duration, and termination; clinical forms.*—However great may be the variations of individual cases, there are certain common features characteristic of amœbic dysentery; these are an irregular course marked by periods of intermission and of exacerbation of the diarrhœa, a tendency to chronicity, and the frequent occurrence of abscess of the liver. Except in the most acute forms, which are often rapidly fatal, one or other of these features is apt to predominate at some period of the illness; or they may be combined in such a way as to produce very varied clinical groups.

For purposes of clinical description, cases may be grouped under one of the following forms:—1. *The grave or gangrenous form*; 2. *Dysentery of moderate intensity* (often showing periods of intermission and exacerbation); 3. *The chronic form.* A similar classification of "tropical" dysentery was adopted many years ago by Dutroulau. It should be remembered, however, that this is but a convenient clinical arrangement; and that cases are frequently observed which do not conform strictly to any one of these divisions: or, again, at different periods of their course, a case may fall now into one group, now into another. For instance, a case of chronic dysentery getting worse may assume the features of the grave form; or a dysentery of moderate intensity may lapse into the chronic form. In temperate climates the second and third forms, particularly the latter, are more commonly met with than the gangrenous form; this may be due to a diminished virulence of the amœba.

The following case exhibits the chief features of the disease:—

George S., aged thirty-five, entered the Johns Hopkins Hospital, January 12, 1891. He had lived in Baltimore many years, and, with the exception of several attacks of chills and fever the last of which occurred ten years ago, had been in perfect health until about midsummer 1890. At this time he had pains in his back, general lassitude, loss of appetite and strength, and occasionally he passed a little blood with his stools. He suffered no further inconvenience until the first week of September when diarrhœa came on, which was severe during two weeks. He suffered no pain, but passed blood and mucus by the bowel, though not in large quantities. Throughout this and the following month the diarrhœa persisted with varying intensity, and about the end of November he began to have severe pain in the abdomen and right side of the chest, and about the right shoulder-blade. Coincidently with this he began to cough and to spit up a blood-stained viscid material. Both the cough and the expectoration were paroxysmal, and his pain was increased when he lay on either side instead of on his back.

During the three weeks previous to his admission to the hospital the diarrhœa had increased in severity; and he had as many as fifteen movements in twenty-four hours, which he described as dark-coloured and watery but containing no blood. He had had no rigors, and but little fever; but occasionally he had sweated profusely, and he had lost much flesh since the beginning of his illness. He stated that he usually drank the water supplied by the city mains; but, on several occasions during the summer, he had drunk water from a spring which was at times contaminated after rains with surface water coming from the "Spring Gardens" in South Baltimore.

Physical examination.—Very weak, emaciated, pale and sallow; dorsal decubitus, no dyspnœa, but frequent hacking cough; temp. 98·6° F., pulse 120, resp. 26. Skin dry and rough, tongue brown and dry in the centre. Thorax: slight bulging of the chest wall behind from the seventh to the ninth rib on the right side, with deficient expansion and partial obliteration of the intercostal spaces. Normal resonance over the right lung in front, and in the axillary space; posteriorly, defective resonance from the spine to the angle of the scapula; below this, absolute dulness with tenderness on percussion and pressure, especially at the posterior axillary fold. Tactile fremitus increased at the base of the right lung. On auscultation, normal vesicular breathing in front and in the upper two-thirds of the axillary space; a few small mucous râles in the lower third. Posteriorly, feeble breathing from the apex to the angle of the scapula, with small râles during inspiration; in the infra-scapular region, during quiet breathing, breath sounds feeble and distinctly tubular with larger and louder râles; these were most marked between the angle of the scapula and the posterior axillary fold; on coughing, the tubular quality of the respiration was accentuated. Left lung normal throughout. Heart sounds clear. Abdomen soft and relaxed, slightly fuller in the right than in the left flank; sensitive to pressure, particularly in the epigastrium, about the navel, and along the course of the colon. The edge of the liver could not be felt distinctly; the lower limit of hepatic dulness extended in the median line to 25 cm. from the navel, and to the same level in the right mammary line; its upper limit was at the ensiform cartilage in the median line, at the upper border of the sixth rib in the right mammary line, and at the lower border of the sixth rib in the mid-axillary line. The spleen was not palpable. Urine scanty and albuminous. Expectoration abundant, very viscid, frothy, of a brownish red colour, containing small, yellowish white, soft, cheesy-looking masses. On microscopic examination, pus cells, red blood corpuscles, alveolar epithelium and hæmatoidin crystals were present. In the sputa examined a few days before the patient's admission to the hospital, amœbæ and elastic tissue fibres had been found: these were again demonstrated.

Diet of milk and egg-albumin. Injections of starch and laudanum. *January 13th.*—Blood count: R. corp. 3,956,000, W. corp. 53,000 per cub. mm. *January 15th.*—Temp. 98° to 101° F.; thirty-five stools in twenty-four hours, liquid, small, very offensive; they contained reddish brown mucus, soft greenish material, and numerous small whitish gray masses. Active amœbæ were abundant. *January 17th.*—Nine stools in twenty-four hours. Sputa 170 c.c. Quinine injections, 1-5000 *bis die.* *January 24th.*—He had been growing weaker every day, and during the last few days had suffered much pain in the abdomen and the right side. The cough was severe, the expectoration ranged from 75 to 120 c.c., the stools were reduced to from 3 to 6 daily, and were passed involuntarily. When the patient was not under the influence of morphia the movements were preceded by great abdominal pain. Amœbæ were constantly present in the fæces and sputa. From the 18th to the 24th the temperature ranged from 99° to 102° F., the pulse from 120 to 150, and the respirations from 28 to 44. Death occurred on the afternoon of the 24th January.

The autopsy revealed extensive dysenteric ulceration of the large bowel, most marked in the cæcum and ascending colon; two large and a number of small abscesses in the liver; consolidation of the lower lobe of the right lung, with a large abscess cavity in its lower portion, and a peculiar sero-fibrinous peritonitis. Actively moving amœbæ were found in the bases of the intestinal ulcers, in the peritoneal exudate, and in the material taken from the abscesses of the liver and lung.

The invasion may be abrupt or gradual. The first mode of onset occurs usually in the grave form of dysentery; though some cases with a sudden and severe onset terminate favourably, or lapse into a chronic condition. The patient is seized with severe colicky pains in the abdomen, and looseness of the bowels; the stools being frequent, thin, and containing mucus and blood. There may be nausea and vomiting, and slight elevation of the temperature—more frequently the temperature is normal. It is with this form of onset that tenesmus is most frequently observed.

The gradual onset is characteristic of most of the cases of chronic dysentery. A painless and not very frequent diarrhœa, alternating with periods of constipation, sets in without any obvious cause—the motions being fluid, of a light yellowish brown colour, and containing mucus, but seldom blood. The patient becomes emaciated, weak, anæmic and sallow. Not infrequently the onset is even more obscure, and the first symptoms may point to disease of the liver; the rational and physical signs being those of suppurative hepatitis. Close questioning, however, will usually elicit an account of an antecedent intestinal disorder, mild and of brief duration, to which the patient may have attached but little importance. In such cases the disease of the liver may be dominant in the clinical picture throughout the illness; but post-mortem records show that, in the great majority of cases, there is more or less extensive ulceration of the large bowel; or scars are present, which testify to an antecedent intestinal ulceration.

The course of amœbic dysentery is very variable; and, as Austin Flint pointed out many years ago, the disease cannot in any sense be considered a self-limited one, as is the case with catarrhal or seasonal dysentery. It presents at irregular intervals the periods of intermission and exacerbation of the diarrhœa, which form so characteristic a feature of the illness, and occur even when the patient is placed under the most favourable conditions for recovery. These exacerbations and intermissions are more specially seen in the chronic cases, and in those of moderate severity; but even the grave form may not run an entirely uniform course, though any abatement of the symptoms is apt to be slight and of short duration.

During the intermissions the patient's general condition is stationary, or there may be a slight gain; but with each successive exacerbation of the diarrhœa there is a further loss of flesh and strength: indeed, it is not till convalescence has been thoroughly established that any material improvement occurs in this respect. Apart from this feature of intermission and exacerbation, the various forms of amœbic dysentery have but little in common from a clinical point of view; the grave cases run a short course with severe abdominal symptoms and early prostration, while chronic cases are met with in which there is nothing more than an irregular diarrhœa, often alternating with constipation, and accompanied by a very gradual loss of flesh extending over months and even years. Yet the ætiological and anatomical basis is the same in both cases, for the amœba is found in both—more sparingly, as a rule, in the latter, it is true—and in both post-mortem examination shows pathological changes of the same nature, differing only in degree. Moreover, the fact noted above, that the same case at different periods may present the features of each of the three clinical forms in turn, is further proof that these phases are manifestations of the same disease.

In keeping with its variable course is the latitude which exists between its extreme periods of duration. The grave cases with abrupt onset last from two to five weeks; cases of moderate intensity from six to thirteen weeks; while chronic cases may extend over months and even years.

The occurrence of complications may shorten or lengthen the duration of the illness. For instance, peritonitis, which is usually due to perforation, is rapidly fatal. Abscess of the liver may protract a case in which recovery seemed to be at hand; or, on the other hand, may bring to an end a chronic dysentery which had lasted many months.

In all but the gangrenous forms the tendency to chronicity is a marked feature, and is one of the gravest elements in the prognosis. The chronic condition may be recognised when the diarrhœa, with or without intermissions, persists for many weeks without pain, and with but slight constitutional disturbance.

Recovery is slow, convalescence being protracted in proportion to the extent and severity of the intestinal lesions, and to the degree of anæmia induced. The earliest indication of improvement is a permanent diminution in the number of amœbæ in the stools; and convalescence may be considered as established when, on repeated examination, the amœba is no longer found in the evacuations. Occasionally there is a temporary return of the diarrhœa and of the amœba, analogous to the exacerbations above mentioned; but it is not accompanied by any material alteration in the patient's general condition.

I have never seen a distinct relapse, although this appears to be of frequent occurrence in cases of dysentery described by physicians in tropical countries; it may possibly be due to a reinfection. It should be borne in mind, however, that dysenteric ulcers are slow to heal, and are often so latent that the cessation of the diarrhœa does not necessarily imply the integrity of the coats of the bowel: the continued presence of amœbæ is a more certain indication of the persistence of dysenteric ulceration, and their absence of its cure, than are the inferential symptoms of the disease.

Death may occur in any stage of the illness. It may result from the gravity of the intestinal ulceration, from exhaustion in protracted cases, from some complication (particularly abscess of the liver, peritonitis due to perforation, hæmorrhage from the bowel, or diphtheritic enteritis), or occasionally from intercurrent disease.

In the gangrenous form the severity of the intestinal lesions or perforation is the usual cause of death; while in the other two clinical forms abscess of the liver, or of the liver and lung, is responsible for the majority of the fatal cases.

II. *Analysis of symptoms.*—(*a*) The gastro-intestinal symptoms predominate in the majority of the cases, being the first to appear and the last to subside. Of these *diarrhœa* is the most important, and occasionally the only one. It varies in character and frequency, not only according to the clinical form of the disease, but also at various periods of the same case.

The exacerbations usually begin suddenly, and subside in like manner, lasting from one or two days to a week or ten days; they are often ingravescent when the illness is approaching a fatal termination. It is not possible to assign any cause for their occurrence; but certainly they are more frequently seen and are of greater duration and severity in the cases complicated with abscess of the liver. The periods of intermission range from one day to three weeks, being shorter or longer in proportion to the extent and gravity of the intestinal ulceration. At such times the stools are soft, even partially formed, and contain a little mucus.

The examination of the stools affords valuable information as to the form and progress of the dysenteric affection. In the grave form the stools are at first very numerous, twenty to thirty in twenty-four hours; but with the advance of the disease they diminish to a dozen or less, and in fatal cases towards the end may not exceed three or four: this diminution is due to the gradual loss of expulsive power brought about by destruction of the muscular coat and the general œdema of the bowel. The earliest stools are in small amount; and consist, after the fæcal contents have been voided, almost entirely of clear or slightly turbid and very viscid masses of blood-stained mucus, mixed with more or less bright blood. The odour is mawkish, and at first not offensive. With the advance of the ulceration the stools become more copious, watery, and less homogeneous; there is less blood, and a good deal of shreddy material of a grayish or yellowish colour appears mixed with the mucus. They contain also small, opaque or translucent, gelatinous, grayish yellow masses, varying in size from a pin's head to a split pea; these are fragments of necrotic tissue from the bases of the ulcers, and they always contain amœbæ. When there is extensive and rapid sloughing, the appearance of the stools is even more varied. They are then greenish (looking like spinach or green scum), grayish, reddish brown (if mixed with blood), or a mixture of these colours; their consistence is watery or pultaceous, and they have a penetrating and horribly offensive odour. Not infrequently they contain large sloughs in the shape of tough, stringy masses of a grayish or brownish colour. The nearest approach to purulency is seen in slimy liquid stools of a grayish colour.

In dysentery of moderate severity with abrupt onset, the stools are at first similar to the earlier motions of the grave form—that is, mucoid and bloody; but if the onset be gradual, or the ulceration established for some time, they become more liquid, brownish yellow, and contain mucus, blood in streaks or small clots, and many of the little gelatinous necrotic fragments noted above. On exacerbation there is, as a rule, an increase of the blood and mucus, and the stools have a more variegated appearance, like those of the grave form.

In the chronic form the stools are homogeneous, being for the most part watery or like thin gruel, of an earthy, yellowish brown colour; they contain few or many flakes of clear mucus, but seldom any blood or necrotic fragments. During an exacerbation, however, the motions resemble those of dysentery of moderate severity.

In the periods of intermission of the moderate and the chronic forms, the fæces become pasty and even partly formed; and the abnormal constituents gradually disappear, except the mucus, which is still found mixed with the fæces, or more generally adhering to their surface. If convalescence ensue the mucus finally disappears, but only after the patient has been passing fully formed fæces for some time.

The reaction of dysenteric stools is usually alkaline, occasionally neutral or amphoteric, rarely acid unless the motions have been left exposed to the air.

Microscopical examination of the bloody mucoid stools shows a large number of red blood corpuscles, a few leucocytes, and a variable number of large round or oval epithelioid cells. The latter often occur in groups; they have a granular protoplasm, a sharp contour, and a round or oval nucleus. In many cases they have undergone fatty or dropsical degeneration. From amœba, to which they bear a close resemblance, they are distinguished by absence of spontaneous movements and by less marked refraction of light. Cylindrical epithelial cells are sparingly found. At a later stage the cellular elements are less numerous, while the amorphous shreddy or granular detritus increases in amount, and elastic tissue fibres are seen. With each exacerbation, however, there is an increase of the cellular elements. In the liquid stools of the chronic form there are comparatively few formed elements except amœbæ.

Crystals of the ammonio-magnesian and earthy phosphates, Charcot's crystals, and occasionally blood pigment, are found.

The organisms present in dysenteric stools are bacteria, flagellated infusoria, and amœbæ. The bacteria most commonly found have already been enumerated in the section on ætiology, and are not peculiar to this form of intestinal flux. They occur sparingly in the earlier evacuations, and become abundant when the ulceration is well advanced. The flagellated organisms—*cercomonas* and *trichomonas*—appear only occasionally and accidentally; but when present are always in great numbers.

The amœba is found in all varieties of the dysenteric stools, and at all periods of illness; but the number fluctuates between wide limits in different cases and at different periods of the same case. The organisms are more numerous in proportion to the extent and severity of the intestinal lesions; that is, in the grave form and in exacerbations of the disease. In the bloody mucoid stools they are in considerable numbers and evenly distributed. In the less homogeneous stools of a later period they are often more numerous and occur in groups; particularly in the little gelatinous necrotic masses, to a less degree in the mucoid portions, and usually singly in smaller numbers in the quite fluid portions of the stools. In the motions of chronic dysentery they are, as a rule, not so abundant, but more evenly distributed. When the fæces are soft and partly formed, they should be looked for in the adherent mucus. Even in stools of the same appearance the number found is far from constant, and this is especially apt to be the case if local treatment has been used. In cases that recover the amœba gradually disappears, though the organisms may be found long after the diarrhœa itself has ceased. Variations in size and activity are often noted. The variation in size is observed in different cases, the amœbæ from any one patient being, as a rule, of a nearly uniform diameter; variations in activity, however, are often observed in specimens drawn from the same stool. The active amœbæ always contain more red blood cells than the sluggish ones; and that the greater activity of the amœba indicates a correspondingly active ulcerative process in the bowel seems to be a just inference. The reaction of the stools, as Cunningham has pointed out, influences the presence and activity of the amœba to a marked extent. In alkaline motions the organisms are numerous and actively motile; in acid ones they are few and only occasionally motile. To obtain the best results in *the examination* *of the fæces for active amœbæ*, attention should be paid to the following points:—1. The stools should be passed into a warm bed-pan, and kept at the temperature of the body until and during the examination. 2. The examination should be made as soon as possible, before the stools become acid. 3. The portions of the stools which usually contain the amœbæ in greatest number should be sought for carefully and examined. 4. The glass slides, cover-glasses, and the stage of the microscope should be warmed.

Of the other gastro-intestinal symptoms *pain* is the most frequent. It is, however, rarely complained of throughout the illness, but is felt chiefly at the onset in the grave form, in the form of moderate severity with abrupt onset, and in exacerbations. It often subsides as the diarrhœa moderates, and even in the terminal stages of gangrenous cases it may be absent. Indeed, ordinary chronic cases are often painless throughout. The pain is cramp-like, tearing or burning in character, and at times so agonising that the patient is unable to lie still for a moment, and keeps tossing about with the hands pressing on the abdomen. It is sometimes localised, particularly in the lower abdominal zone; but more frequently it is general, and tends to occur in paroxysms which precede and accompany a movement of the bowels, subsiding gradually after the stool has been passed. In chronic cases a dull aching or a feeling of heaviness about the epigastrium is much more common than colicky pain. The abdomen is commonly flaccid and somewhat retracted. On palpation it may feel doughy, and sometimes, when the abdominal wall is thin, the thickened intestine can be distinctly felt, especially on the left side. Sensitiveness to pressure, though often present, is rarely extreme even in extensive ulceration; it is elicited mainly along the course of the large bowel.

Tenesmus is not prominent in most cases of amœbic dysentery, though it is described as being characteristic of dysenteric ulceration in general. Dutroulau, however, who had a very large experience of dysentery in the tropics, insisted that it was not a common symptom in the cases he had observed. It is met with chiefly in those cases of dysentery in which the rectum is ulcerated, and this part of the bowel is not frequently involved in the amœbic form. In the grave cases, however, marked by extensive sloughing, it is not uncommon. A burning sensation about the anus during and after defecation is more generally present.

Nausea and vomiting are uncommon except as initial symptoms, or in cases complicated by abscess of the liver and lung; in the latter case they are apt to follow paroxysms of cough. *Hiccough* has been noted in the terminal stages of the gangrenous form, and when the peritoneum becomes involved. *Loss of appetite* occurs early and is absolute in the acute cases; and throughout the illness there is a more or less pronounced distaste for solid food, but on the other hand a craving for fluids, which is readily accounted for by the continued drain from the intestine. In cases of moderate severity the *tongue* is flabby, and covered with a more or less thick white fur: in fatal cases it becomes dry, brown and fissured, and in chronic cases may be little altered from the normal.

(*b*) *Fever* is not a marked symptom in this form of dysentery, though a moderate elevation of temperature is usually present at some period of the twenty-four hours daily throughout the illness. In the terminal stages of fatal gangrenous dysentery, when the patient is collapsed, the temperature is often continuously normal or even subnormal, and chronic cases continue for weeks without any fever. Exacerbations of the diarrhœa are sometimes attended by a slight increase of the fever; but persistent elevation of the temperature is undoubtedly most frequently due to abscess of the liver, or of the liver and lung; and may occur long before there is any local evidence of hepatic or pulmonary mischief. The temperature curve is irregular, consisting of alternations of continuous remittent and intermittent pyrexia. In the main the fever is of the septic type with a small range—from 99° to 101° or 102° F. With the onset of abscess-formation in the liver the temperature tends to become more regularly intermittent. The fever declines during convalescence, but slight recrudescences occur even when the diarrhœa has ceased. Distinct rigors are rare, and occur only in cases complicated by abscess of the liver. Sweating, on the contrary, is observed in all the abscess cases, and in the collapse following a severe attack of gangrenous dysentery. In the former case it is paroxysmal, and may or may not be preceded by a slight chilliness; in the latter the skin, particularly of the extremities, feels cold and is constantly covered with a fine clammy sweat.

(*c*) The *skin* in chronic cases is usually dry or even scurfy. With this is associated a peculiar sallowness or earthy tint which, as I have elsewhere remarked, resembles that of dirty chamois leather, and is most evident on the face.

(*d*) More or less *anæmia* appears in all cases of amœbic dysentery in proportion to the severity of the infection or the duration of the illness. There is a deficiency both in the corpuscular elements and in the hæmoglobin; and the state of the blood in the main is that observed in a secondary anæmia however produced. There is no doubt that the anæmia is due to the action of the amœbæ themselves; for, as I have said in the section on ætiology, they are very frequently found loaded with fresh red blood cells, especially in acute cases—in other words, whenever there is evidence of progressive intestinal ulceration. To this principal cause must be added the direct loss of blood due either to capillary oozing from large areas of ulceration or, more rarely, to the profuser hæmorrhage resulting from the erosion of blood-vessels. In the more protracted cases the malnutrition brought about by the prolonged gastro-intestinal disturbance keeps up and even increases the anæmia.

(*e*) The *pulse and respirations* during the greater part of the illness follow the variations of the temperature. In cases of moderate severity the pulse ranges from 80 to 90 or 100; in the grave form from 100 to 110, or more; in chronic cases there is usually a pulse of normal rate. In the collapse, however, which ushers in the fatal stage of gangrenous dysentery, the pulse becomes very rapid—120 to 140 or more, thready and compressible; and this occurs usually with a fall of the temperature below the normal. The respirations increase with the pulse, unless in the collapsed condition, in which they may be shallow and infrequent; and in cases of abscess of the liver and lung, in which they are accelerated out of proportion to the pulse rate.

(*f*) Slight *albuminuria* is of frequent occurrence even in cases which are not severe; and hyaline casts are occasionally found in the urine. Retention of urine occurs in the grave cases, and the quantity withdrawn by catheterisation is usually much below the normal amount. In none of the cases which I have had under observation was there any vesical tenesmus.

III. *The complications* which have been observed in the course of amœbic dysentery, though not many, are important. They are occasioned either by the extension of amœbic infection to structures other than the intestine, or by the progressive destruction of the intestinal tunics. To the former class belong abscess of the liver and of the liver and lung; to the latter, intestinal hæmorrhage and peritonitis, with or without intestinal perforation. In all of these amœbæ, with or without the aid of associated microbes, are the active agents. There is one complication, however, of comparatively rare occurrence, in which the amœba plays no part, which is due to the exclusive action of bacteria; namely, diphtheritic inflammation of the intestine. Indeed, the rarity of this pathological process in amœbic dysentery is in itself an argument for the separation of the amœbic form from other forms in which diphtheritic inflammation is the rule and not the exception.

Of the many other complications enumerated as occurring in the course of "dysentery" in general, I have not seen any examples in the cases of amœbic dysentery, either in the cases which I have personally observed, or in those recorded by others.

Abscess of the liver, or of the liver and lung, is by far the most frequent and important of all. An examination of the principal statistics shows that, in tropical countries at least, one in every four or five cases of dysentery is accompanied by abscess-formation in the liver, and that the mortality from dysentery is largely due to this complication. In many cases, indeed, the hepatic disease forms the principal part of the clinical picture, and may even appear to precede the intestinal disease. [To avoid needless repetition, the reader is referred to the article in the next volume on Amœbic Abscess of the Liver and of the Liver and Lung under the general head of Diseases of the Liver; where the symptomatology, pathological anatomy, and certain debated points in the ætiology of this malady are treated in detail.—Ed.]

Intestinal hæmorrhage is not of frequent occurrence, which is the more remarkable in view of the extensive destructive lesions which are present in the majority of the cases. This is to be explained by the thrombosed condition of the blood-vessels in the zone of infiltration and œdema which surrounds the intestinal ulcers, and by the notable absence of inflammatory reaction with its attendant vascular congestion. In one case observed by myself 125 c.c. of clotted blood were passed per rectum; but here a diphtheritic inflammation was added to amœbic infection. The symptoms produced by this complication are those of more or less rapid collapse, according to the quantity of blood effused.

Intestinal perforation, next to abscess of the liver, is the most important complication; it appears to be uniformly fatal. It occurs most frequently in grave or gangrenous cases, where there is necrosis of large areas of the intestinal wall. The thin and necrotic bases of the ulcers give way, large rents or holes in the bowel are formed, and the intestinal contents are soon distributed throughout the peritoneal sac. There is often more than one perforation. If the patient live long enough after this accident an acute general peritonitis is the result; but frequently the shock is so great that death ensues in a few hours, before there is time for inflammatory reaction. The symptoms and physical signs differ in no way from those of intestinal perforation, however induced; and owing to the extreme weakness of the patient are often indefinite. As in the case of perforation in typhoid fever, however, sudden collapse with a subnormal temperature is, even in the absence of abdominal pain, a highly suggestive sign—if massive intestinal hæmorrhage can be excluded.

Judging from the frequency with which peritoneal adhesions are found in autopsies of persons who have died of amœbic dysentery, it is certain that *localised peritonitis* without perforation is not uncommon; and, as stated in the section on pathological anatomy, the peculiar kinks in the bowel appear to be due to the same process affecting contiguous portions of the visceral peritoneum. However, evidence of these conditions in life is seldom present, and clinically these forms have but little importance. It is difficult to distinguish the abdominal pain and sensitiveness in such cases from that which is present to a greater or lesser degree in all cases with severe intestinal ulceration.

Diagnosis.—In most cases the diagnosis is readily made by the detection of actively motile amœbæ in the stools; and a single examination in a well-marked case of amœbic dysentery usually affords this positive evidence.

Repeated examination, however, may be required in chronic cases, where the amœbæ are often few and sluggish; especially if the evacuations consist of partially formed fæces with small quantities of adherent mucus. Again, when rectal injections have been used in a case of intestinal flux of doubtful nature, no positive conclusion can be drawn from the absence of amœbæ in the stools first passed; for the organisms, if present at first, are quickly destroyed by such injections: but, if the local treatment be discontinued, they may reappear in the later evacuations.

It is absolutely essential to the successful examination of the stools that the various points in the technique, described in a former section, be carefully attended to; otherwise the amœba may be entirely missed, even after a prolonged search. This is particularly the case when the examination has been delayed, and the material allowed to fall below the temperature at which the amœba is actively motile; though to the practised eye even motionless amœbæ are easily distinguishable from other cellular elements by their circular outline and strong refraction of light.

In some cases the diagnosis of the intestinal disorder can be definitely established only by finding amœbæ in the aspirated contents of a liver abscess, or in the sputa when the abscess has invaded the lung, and is discharging itself through a bronchus. [See Amœbic Abscess of the Liver and Lung, vol. iii.]

By the detection of actively motile amœbæ it is possible to exclude other acute and chronic forms of intestinal flux; such as diphtheritic colitis, catarrhal (seasonal) dysentery, typhoid fever, tubercular enteritis, and acute and chronic diarrhœas of various origin. In rare cases, however, there may be a double infection, as in the case of diphtheritic colitis previously mentioned; or in the cases of Kruse and Pasquale, in which there were tubercular ulcers along with the lesions of amœbic dysentery.

Reference has already been made to the earlier observations of Cunningham, Massiutin, and others, who claimed to have found amœba in cholera, acute and chronic intestinal catarrh, typhoid fever, and other intestinal diseases; and the opinion was then expressed that, in the light of our present knowledge, many of these cases may well have been amœbic dysentery. In the remaining cases it is highly probable that the amœbæ were identical with those which Schuberg occasionally found in the normal intestine, and Kruse and Pasquale proved not to be pathogenetic in cats. In a doubtful case the inoculation of cats with the material containing amœba should be practised according to the method described in the section on ætiology. In this way it will be possible to distinguish the harmless from the pathogenetic variety, between which no morphological distinctions have hitherto been discovered. I have examined many cases of looseness of the bowels in various diseased conditions, and only once have succeeded in finding amœba in a case which did not ultimately prove to be amœbic dysentery. This was a case of malignant disease of the stomach in which the light yellow fluid motions contained many active amœbæ. No ulceration of the bowel existed; unfortunately no inoculation experiments were made, as the case came under my observation before the publication of the researches of Schuberg, and Kruse and Pasquale.

The direct evidence derived from the examination of the stools is further strengthened by the history and course of the illness. The irregular diarrhœa, beginning gradually or abruptly with bloody mucoid stools, presenting periods of exacerbation and intermission, and accompanied by fever, emaciation, and sallowness, is highly suggestive of this form of dysentery; and if to these phenomena are added the signs of abscess-formation in the liver and lung, a sufficiently characteristic clinical picture of amœbic dysentery is afforded. In uncomplicated chronic cases the chief diagnostic features are the continued presence of amœbæ in the stools and the characteristic cachexia.

Prognosis.—In a disease which runs so variable a course, which is frequently attended by serious and often fatal complication, and has a constant tendency to chronicity, the prognosis is necessarily uncertain from the outset. Most of the grave cases become so by progressive exacerbations, and a mild onset is consequently no indication of a favourable course. Moreover, abscess of the liver and lung occurs quite frequently with such a mode of onset; and, as I have already said, this complication is responsible for a large proportion of the fatal cases. In the gangrenous cases an unfavourable issue is imminent from exhaustion or perforation of the bowel with peritonitis; in cases of moderate severity from infection of the liver and lung; while in the chronic form the same result is often brought about, after the lapse of many months, by the continued cachexia, even if the occurrence of abscess do not lead to a speedier termination.

In uncomplicated cases recovery may be expected when the fæces become formed, and are pronounced after repeated examinations no longer to contain amœba.

Until some means be discovered of destroying the amœba in the deeper layers of the bowel the prognosis must be uncertain.

Treatment.—1. *Prophylactic.*—If it be granted that amœbic dysentery is an infective disease due to a specific organism, it follows that the adoption of proper prophylactic measures should produce a large decrease in the number of cases where the disease is epidemic. Unfortunately the life history of the amœba outside of the human body is unknown, and the sources of infection cannot therefore be definitely controlled. We may suppose, however, that purification of the water-supply would do away with a likely source of infection. Though there is little risk of infection by the dejecta of dysenteric patients, it is advisable that these, and any articles soiled by them, be rendered innocuous by the addition of a weak solution of carbolic acid, or of milk of lime; the amœba is rapidly destroyed even by feebly antiseptic agents.

2. *General, Dietetic, and Symptomatic.*—The measures to be adopted are similar to those which have been found suitable in other forms of intestinal flux. The patient should be confined to bed, even in chronic cases with little constitutional disturbance; in acute cases no persuasion will be required. As in other diseases attended by looseness of the bowels, the effect of this step is usually to diminish very materially the number of evacuations, and to husband the patient's strength for what is often a long and wasting illness. For the same reason, and to facilitate the examination of the dejecta, the bed-pan should be used exclusively; though many patients feel a difficulty at first in passing their motions in this way.

Milk is the staple diet, but may be supplemented by other liquid foods, such as clear soups, thin gruel, or whey. If lumps of curd are found in the stools the milk is to be diluted or partially peptonised. When there is much intolerance of food diluted egg-albumin may be given for a few days. Whatever be the food, it is advisable to give it in small quantities at frequent intervals. Such a dietary must be continued until the subsidence of the disease, and during convalescence the return to a full diet is to be made very gradually.

Abdominal pain is the symptom which most frequently calls for treatment. It is often relieved by external applications, such as fomentations or turpentine stupes; but it may require the use of opiates, preferably by subcutaneous injection. Pain in the lower portion of the bowel, and tenesmus, are most speedily relieved by enemas of starch and laudanum, or by cocaine suppositories; the same measures serve to dispel the insomnia due to frequent and painful motions.

When convalescence has been established some ferruginous preparation is required to overcome the anæmia which is invariably present.

3. *Curative.*—(*a*) Many remedies have been used for the treatment of "dysentery" in general; and the list is increasing every year. It is certain that many of the cases recorded as cured have been examples of catarrhal dysentery, which is common at certain seasons of the year in nearly every part of the world, and is a self-limited disease, subsiding spontaneously under or in spite of any treatment.

In amœbic dysentery the substances chiefly relied upon to modify or arrest the pathological process have been quinine, calomel, and the intestinal antiseptics generally. We may assume that agents which readily destroy the amœbæ outside of the body would probably have the same effect on the amœbæ in the tissues. The literature of this form of dysentery, however, is as yet too scanty to furnish conclusive evidence of the value of any of these agents.

I have used quinine (5 grs. three or four times daily) in six cases without being able to satisfy myself that any good resulted from its use. Possibly if pushed in larger doses a favourable effect might be produced.

Calomel (0·05 grm., two to six times daily) was used by Quincke in two cases of chronic amœbic dysentery, with the result that the amœbæ diminished in number but did not entirely disappear.

Salol and bismuth have also recently found advocates.

Ipecacuanha, which has so long been the mainstay in the treatment of dysentery in India, has not had an extended trial in the amœbic form. In the single instance in which I administered it, no effect, beneficial or otherwise, could be detected. It is very desirable that the merits of this much-extolled specific should be tested in India in cases which have been shown unquestionably to be of amœbic origin.

Maberly, practising in South Africa, has obtained good results in dysentery with a tincture of the Monsonia ovata, prepared from two and a half ounces of the dried flowering plant or root to a pint of rectified spirit, given in doses of two to four drachms every four or six hours. It is claimed for this drug that, while therapeutically equal to ipecacuanha, it produces no unpleasant effects. These claims, supported as they seem to be by a somewhat extensive experience, deserve further investigation.

(*b*) Local treatment by means of rectal injections, or by irrigations of antiseptic solutions, commends itself as being the most rational and direct method of medication; and the results achieved, though not brilliant, warrant a further trial. The advantage of treating a local disease by local means is obvious; and the fact that the amœba is susceptible to the action of solutions so dilute as to be only feebly toxic gives us a stronger hope of the success of this method. Solutions of quinine, corrosive sublimate, nitrate of silver, and nitric acid have been chiefly used.

The use of quinine injections in dysentery was revived by Lösch, who found that the amœba is destroyed by a solution of 1-5000. Stronger solutions (1-2500, 1-1000, and even 1-500) may be injected with impunity three or four times daily; and the small amount absorbed by the intestine may have a similar effect on the amœbæ in the tissues.

Corrosive sublimate is used in a strength of 1-5000 or 1-3000, and nitrate of silver in a strength of thirty grains to a quart of water. These solutions must be used with greater caution than the quinine solutions.

I have had no experience with the dilute solution of nitric acid, which, by reason of its astringent action and the great susceptibility of the amœba to acid media, would appear to be a very suitable agent.

From one to two pints of one or other of these solutions are used three or four times daily. The injection is made slowly, so as to cause the least possible discomfort, and the patient is directed to retain it if possible fifteen minutes, gentle friction being meanwhile practised over the course of the bowel with the object of diffusing the fluid throughout the whole of the affected area. The passage of the enema is facilitated by raising the hips on a pillow or, if the patient's condition permit, by placing him in the knee and chest position. If the rectum be very irritable a cocaine suppository is introduced a few minutes before the injection is given. This treatment should be persevered in daily until no more amœbæ appear in the stools. To judge of the effect the injections should be suspended for a couple of days from time to time, and the fæces carefully examined during this interval. If amœbæ be still present the injections must be resumed.

In gangrenous cases little good can be expected from such treatment; there is some risk, indeed, that the injections may precipitate a perforation of the bowel. In such cases small sedative enemas are better tolerated, and they afford considerable relief.

If the injections do not reach the amœbæ embedded in the tissues, they may, by destroying those lying in the ulcerated surfaces and in the lumen of the bowel, at least prevent the infection of the intact portions of the intestine.

4. *Treatment of Complications.*—[For the treatment of abscess of the liver and lung, see Amœbic Abscess of the Liver and Lung, vol. iii.]

Perforation of the bowel is a hopeless condition. On account of the extensive disease of the bowel found under such circumstances, there is even less prospect of success from surgical intervention than in a similar accident in typhoid fever. The best that can be done is to allay pain by subcutaneous injections of morphia.

Local peritonitis without perforation calls for the administration of opiates and the application of fomentations or turpentine stupes.

Massive hæmorrhage also is best treated by the judicious use of opium, which quiets the circulation and reduces peristalsis to a minimum. An ice-bag may be applied to several portions of the abdomen along the course of the large intestine.

HENRI A. LAFLEUR.

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H. A. L.

INTOXICATIONS

POISONING BY FOOD—PTOMAINE POISONING
GRAIN POISONING
MUSHROOM POISONING
SNAKE-POISON AND SNAKE-BITE
ALCOHOLISM
OPIUM POISONING, AND OTHER INTOXICANTS
METALLIC AND SOME OTHER FORMS OF POISONING: INCLUDING POISONOUS TRADES

POISONING BY FOOD—PTOMAINE POISONING

Food may act as a poison in two different ways: the poisonous qualities may be imparted to it by various forms of bacteria; or chemical poisons, whether inorganic substances such as arsenic or antimony, or organic substances such as alkaloids, may be mixed with the food. This latter kind of food poisoning belongs to toxicology, a department of medicine not included in this work. The first form of poisoning is one which comes more directly under clinical observation, and to it the subsequent remarks will be chiefly confined.

For practical purposes food poisoning due to bacteria may be considered under three headings:—

1. Before being eaten the food may have undergone putrefactive changes, with the formation of poisonous chemical substances. The symptoms in this case are of rapid onset.

2. Putrefaction may not have occurred, but the food may contain pathogenetic micro-organisms which, when swallowed, set up symptoms of poisoning. These cases, like the infective diseases, are characterised by a period of incubation; and not infrequently they produce special local lesions elsewhere than in the gastro-intestinal tract.

3. Putrefaction may not be present in the food when swallowed, but putrefactive processes in the food may subsequently occur in certain conditions of the small and large intestine, and produce toxic symptoms which bring this class of cases into close relation with the first class.

In two of these classes of cases, therefore, putrefaction of food plays an important part; and, in order to explain the symptoms produced, it is essential to understand clearly the decomposition of food by putrefactive organisms. The third class of cases, in which certain micro-organisms taken with the food produce a specific disease, are of great importance; and, although not yet thoroughly worked out, many facts which indicate such a series of events have been observed.

Putrefactive processes.—Putrefaction is a process in which various micro-organisms acting on proteid substances split them up into chemical substances, some of which are poisonous while others are harmless. The micro-organisms are of two kinds, aerobic and anaerobic; the former require oxygen for their growth, the latter grow best in the absence of oxygen. The complete morphology of the putrefactive bacteria is not yet known, and this is not the place to discuss it. Of more practical interest are the substances which are formed from proteids during putrefaction, as these are the substances which produce the symptoms in food poisoning. Gases are formed, such as carbonic acid, hydrogen, nitrogen, sulphuretted hydrogen, and marsh gas (C_2H_4); also acid bodies, such as formic, acetic, butyric, and valerianic acids, and lactic, succinic, glutamic, and aspartic acids; and again ammonia and amine bodies, such as trimethylamine. To this last group belong the animal alkaloids or ptomaines. Other substances are present in varying quantities; these belong to the aromatic series, such as indole, skatole, tyrosine, and the like, while in an early stage of putrefaction albumoses are formed from the proteids.

Of these substances the most poisonous are those belonging to the group of amines and of ptomaines. Ptomaines, which were first studied by Selmi, were the subject of extended research by Brieger. From decomposed beef and horse-flesh Brieger separated several alkaloids—neuridine, neurine, choline, and one apparently identical with muscarine, the active principle of amanita muscaria. From decomposing horse-flesh an alkaloid was separated which in its physiological action resembled curare; it acted, that is, as a paralyser of the motor nerve-endings. From decomposing fish trimethylamine, dimethylamine, methylamine, neuridine, cadaverine and putrescine were separated. The physiological action of these alkaloids is of very varying intensity. Some, such as cadaverine, putrescine, and choline, are but slightly poisonous; others are extremely toxic, and cause death rapidly. The action of these is exerted partly on the digestive tract and the secretions poured out into it; partly on the nervous system, and partly on the heart. The muscarine-like alkaloid, separated by Brieger from decomposed flesh, causes profuse diarrhœa, salivation, lachrymation, and sweating; the respiration is also affected, and in large doses clonic spasms appear along with the signs of cardiac failure. Neurine and choline, although they are much less poisonous, possess a similar action. Neurine is more toxic than choline. Mydaleine, which has been obtained from the human cadaver, possesses a similar physiological action; but it also causes a rise in temperature and dilatation of the pupil, and tends to produce paralysis as well as convulsions.

Sepsine, which was obtained by Bergmann and Schmiedeberg from decomposing yeast, causes vomiting and bloody diarrhœa. The extract of putrefied maize is said to possess substances which are narcotic or tetanising, while an alkaloid resembling atropine in its action has been separated from decomposing animal matter (quoted by Brunton).

In most instances, therefore, the effect on the nervous system of these alkaloids is well marked; and may be shown not only by a general depression of the mental and bodily faculties, but also by definite palsy, by convulsions, or by coma. Another characteristic of cases of "ptomaine" poisoning is the association of these nervous symptoms with the signs of gastro-intestinal irritation and of cardiac failure; the whole being an acute process.

Of causation of the fever in these cases we have no definite knowledge. With the exception of mydaleine, none of those substances produces a rise of body temperature. The other substances present, which are fever-producers, are the albumoses or digested proteids; and it is quite possible that these latter are the febrile agents: this possibility is strengthened by the fact that the fever is more intense at the early period of the illness, and that the albumoses are formed from the proteids during the early stage of putrefactive decomposition. The putrefactive processes which occur in the intestines, under the conditions presently to be discussed, no doubt yield toxic products resembling those just described. In these cases the food itself has not necessarily undergone putrefaction when taken.

Food as a source of poison.—Food may serve as a poison in three ways: (i.) by putrefactive changes occurring in it; (ii.) by means of specific bacteria contained in it; and (iii.) food products (animal and vegetable) may become poisonous by way of the soil in which vegetables are grown, or in the case of animals by means of their food or by disease.

(i.) and (ii.) The severest epidemics of food poisoning have not occurred as the result of meat actually "putrefied"; that is, of meat which can readily be recognised as putrefied by the smell. In most cases, indeed, meat in such a condition would be rejected as food. Moreover, it is known from experiment that the most toxic products of putrefaction are present in the earlier and not in the later (foul-smelling) stages of the process. Putrefaction is indeed a somewhat vague term when applied to the changes which are due to certain ill-defined bacteria. These "putrefactive" bacteria are individually present in varying proportion in putrefying liquids. Bacteria, more particularly the pathogenetic forms, in their action on proteids form specific products the toxicity of which varies, as well as do the particular lesions found in the body after death. These facts bring the cases of poisoning by "putrefactive" food into scientific relationship with those cases in which specific micro-organisms and specific lesions have been found.

One of the best-known examples of the kind was investigated by Dr. Ballard, of the Local Government Board (*Report of Medical Officer for* 1888): it is known as the Middlesbrough epidemic of pleuro-pneumonia. Pneumonia of a distinctly infective type, that is, communicable from person to person, existed in the town, and was curiously limited in its geographical extent. The investigation by Dr. Ballard clearly traced the source of the epidemic to the use of "American bacon," which was made by "soaking in water and then only slightly drying salted pork imported from America." This bacon was proved to be poisonous to animals fed with it, and lung lesions were produced. A short bacillus was found by Dr. Klein in the affected parts of the body.

The Middlesbrough epidemic of food poisoning is to be looked upon as the result of the ingestion of a pneumonia-producing micro-organism [*vide* article on "Epidemic Pneumonia"]. As a rule, however, the specific lesions produced by the micro-organisms which cause epidemics of food poisoning are chiefly limited to the gastro-intestinal tract. In the stomach and intestines there is evidence of intense inflammation, frequently with submucous ecchymoses; while the lungs, liver, spleen, and kidneys are engorged with blood. As a rule there is no pneumonic consolidation. Dr. Ballard, in a review of fourteen instances in which disease of a specific character was spread by means of infected articles of flesh food (*Report of Medical Officer of Local Government Board*, 1890-91, p. 189), draws attention to the fact that in most cases the infected food has been pig meat of one kind or other. Thus, of the fourteen instances, the food was pig meat of one kind or another in ten; veal, one; beef, one; butcher's meat (kind unstated), one; and in one instance tinned salmon. In discussing the origin of the infection in these cases, Dr. Ballard points out that it appears to be "accidental." For example, in the Middlesbrough epidemic, bacon, similarly prepared to that which caused the disease, was eaten in the neighbouring districts with impunity; and in another epidemic one joint proved infective, while the rest of the carcase was harmless. Another important point in these cases is that the outbreaks almost invariably occurred from food which had been prepared a day or so before being eaten—as if the infective micro-organism had gained access to the food after it had been cooked. As regards the peculiar liability of pig meat—whether in the form of cold pork, pork pie, sausage, or brawn—to cause food poisoning, Dr. Ballard suggests that it may possibly be connected with the large amount of gelatine which is formed during the process of cooking pig meat; as gelatine is an excellent culture medium for the bacteria. There is probably a great deal of truth in this suggestion; and Dr. Ballard quotes the case of the Nottingham outbreak (*op. cit.*), in which there was evidence that it was not the hot pork which caused the poisoning, but the gelatinous stock or gravy which was simply warmed and served with it.

In some epidemics of food poisoning it has been shown that the food was poisonous at one time and innocuous when eaten later; or that one part of the food was poisonous and another harmless. The latter condition is readily understood; but, in the first case, it must be supposed that the bacterium dies after a time, and the food becomes comparatively harmless.

Symptoms of food poisoning.—In poisonous foods of the kind just discussed, toxicity may depend on two factors: on the bacterium itself, and on the chemical products of its activity. This combination is not without its practical significance; the action of the chemical poisons produces symptoms soon after the food is eaten; but for the effect of the bacterium itself a period of incubation—a period, that is, during which it is growing and producing toxic chemical substances—is necessary. In some cases, therefore, the onset of the symptoms is rapid; in others, it is delayed for several hours. The period of incubation varies in different epidemics, and depends no doubt on the nature of the micro-organism, and on the number present in the food. In the Middlesbrough epidemic the incubation period was eighteen to thirty-six hours; in other instances the period before the onset of symptoms varied between four and forty-eight hours—the shorter period occurring, no doubt, in those cases where the poison was chiefly chemical, the longer in those where the poison was chiefly bacterial. The onset is almost invariably sudden. Directly after partaking of the poisonous meal the individual feels no bad effects and proceeds to his work, but is soon seized either with a rigor, with faintness and muscular weakness, or with abdominal pain. Vomiting may ensue, and giddiness; and diarrhœa, sometimes with bloody and offensive stools and great thirst, is an almost invariable and a prominent symptom. The patient soon becomes febrile, and the rise of temperature varies considerably. As the case progresses the symptoms referable to the heart and to the nervous system become well marked. With the great bodily prostration there are a rapid pulse of low pressure, muscular twitchings, dilatation of the pupil, disturbances of vision, and drowsiness. Suppression of urine may occur, as well as a rash on the skin, sometimes urticarial, sometimes erythematous in character. Convalescence may be tedious; death occurs usually in coma.

Treatment.—The object of treatment is first of all to get rid of the poisonous material from the intestinal tract. If the case be seen in the early stage, a purgative may be administered; either castor oil (1 ounce) with 5 to 10 minims of tincture of opium, or 3 to 5 grains of calomel. In the stage of profuse diarrhœa purgatives, as a rule, are harmful, and the exhibition of sedatives with intestinal antiseptics is necessary. Opium or morphine may be used as sedatives unless there be a tendency to coma; and as intestinal antiseptics salol or beta-naphthol—5 grains every two hours—may be given. Hydrargyrum cum cretâ in small doses (½ to 1 grain) every four hours is beneficial in mild cases; and belladonna or atropine may be tried as an antidote. Stimulants are usually necessary to counteract the prostration and the cardiac failure; and the diet is to be a strictly liquid one, consisting chiefly of milk that has been boiled, and, to a less extent, of beef tea.

(iii.) **The poisonous properties acquired by food,** whether, as in the case of vegetables, it be from the soil or disease during growth, or from the food or disease of animals supplying food products, need little discussion here. In the latter class would come tuberculous meat, meat containing parasites (more particularly trichina), and meat obtained from animals suffering from acute disease. In the last case such meat has been known to produce vomiting, diarrhœa and general prostration with fever. The meat of cattle suffering from cattle-plague must be considered as harmful; while that from cases of epidemic pleuro-pneumonia and foot-and-mouth disease is probably harmless. In anthrax and in symptomatic anthrax (black-quarter) the meat is dangerous.

Milk may be harmful by containing pus or tubercle bacilli; or, after being drawn, it may become contaminated with the poisons of scarlet fever, diphtheria, or typhoid fever.

As regards vegetables the most important examples are ergotism and of poisoning by mushrooms. The reader is referred to the special articles on these subjects.

Putrefaction in the Intestines. — Putrefaction, not directly associated with any change occurring in the food before it is eaten, or with the presence of any specific bacterium, may occur in the intestines. In such cases some local condition of the intestines leads to the putrefactive change; and since the putrefactive products produce symptoms of poisoning, which by clinical observers are frequently spoken of as "ptomaine" poisoning, this condition must be referred to here.

i. In some cases the putrefactive change is associated with the retention of the digesting food in the small intestine, or of fæcal matter in the colon. This putrefaction with its attendant symptoms may be mild, as when there is no organic obstruction to the onward passage of the intestinal contents; but it becomes a well-marked feature when there is organic obstruction from whatever cause (intestinal obstruction, hernia, etc.) Such cases occur in children and adults, and are characterised by fever, by great prostration and collapse, and by a rapid low-pressure pulse.

ii. In other cases putrefaction is associated with specific diseases of the intestines, more especially with typhoid fever, dysentery, and "tropical diarrhœa."

Sidney Martin.

GRAIN POISONING

Rare and indeed virtually unknown as are the grain intoxications in our own country, I might well have been content with a brief reference to them. But the pathological interest of these cases is very great, both from a clinical point of view and from that of the experimental pathologist.

The damage done by the use of musty grain as food falls upon the nervous system, and above all upon the spinal cord; and herein we shall see the usual tendency of disease to attack this structure in sections; moreover, the influence of this part of the central nervous system upon nutrition is in no disease more remarkable. The effects of vaso-motor disorder are also evident; though it is not quite clear how far this is primary or, on the other hand, secondary to irritation in the cord. The parallels between the effect of the grain poisonings and certain forms of spinal disease more common among ourselves are also very instructive. It is much to be desired that highly competent observers should be entrusted with the duty of investigating such epidemics so long as they occur—a time, we trust, of no great duration; for their occurrence in all cases is a sign of degraded and grievous conditions of life. That Raynaud's disease, acrodynia, and erythro-melalgia may be illustrated by the events of grain poisoning is indicated hereafter. There are three well-known modes of grain poisoning: A. Ergotism; B. Pellagra; C. Lathyrism.

A. Ergotism.—Germ. *Kriebelkrankheit.*—The formidable labour of searching into the records of ergotism was scarcely begun when a little book on the disease by Dr. Edward Ehlers of Copenhagen fell into my hands. I do not pretend to have submitted the work of Dr. Ehlers to any critical examination, but the essay has a scholarly method and style, it contains a bibliography of 153 entries, and to judge from the text, these references, or most of them, have been verified and consulted. The only unscholarly feature about the book is that it is published without date,—a practice which is not only annoying, but also immoral; we may attribute the device to the publisher, and, meanwhile, as the last entry in the list of references is dated 1894, we are well up to date. Until I read this treatise I had an imperfect conception of the terrible scourge of ergotism in mediæval times. It seems that ergotism has never been widely prevalent in Great Britain: in Dr. Ehlers' list I see the names of English physicians scarcely appear. The reason is, no doubt, that the English peasantry was never in so wretched a plight; and meat entered far more largely into the common diet. In France, on the other hand, in Central Europe, in Russia (not to pass into the East), perhaps few plagues have been more destructive—none certainly more laden with torture. Montaigne tells us, of the bubonic plague in his own time, that while, as a philosopher, he forbore to give way to personal fears, he felt the less agitated by its presence as he saw in it a not dreadful mode of death, but one rapid and mercifully casting its victim into a torpor from the beginning. "C'est une mort qui ne me semble des pires; elle est communement courte, d'étourdissement, sans douleur, consolée par la condition publicque, sans cérémonie, sans dueil, sans presse." The plague of ergotism, on the contrary, seems to have been a torture as slow and excruciating as it was ruthless. But ergotism was not likely to penetrate into the château of Montaigne: ergotism was a disease of the base people; and even in the plague time its owner did not feel that it was the duty of a philosopher to put himself in the way of infection, not even if the philosopher were also Mayor of Bordeaux.

Although this work is not concerned with the historical aspects of medicine, yet a very brief account of the story of ergotism, as we learn it more fully from the pages of Dr. Ehlers, may not be out of place. Passing over the conjectural matter—such matter, for example, as the possible reference to ergotism in several places in the Old Testament; or, again, in Hippocrates and the Arabians—we come to a pestilence which was called "ignis sacer" by the chroniclers of the tenth to the twelfth centuries. This grievous disease at a later date was called "St. Anthony's Fire"; but under this name certainly more than one disease was included, especially erysipelas; which, indeed, was probably regarded, even by the physicians, as but one of the forms of the disease we now know to have been ergotism. Nomenclature was loose enough in the twelfth century. That St. Anthony's fire was often ergotism, at any rate, is almost proved by a woodcut reproduced by Dr. Ehlers, from Gersdorff (14), in which the saint is adored by a man who has lost his right foot; while his left hand, which he raises towards the saint, is represented, not as swollen, distorted, or ulcerated, but as burning with a living flame. Gersdorff entitles his chapter "Von dem heyssen Brand, den man nennet sanct Anthonius fewr." St. Martial was also more or less concerned with the pestilence. Syphilis, and other gangrenes, ulcers, and witherings, were, of course, confounded with ergotism and with one another; as I have pointed out elsewhere in discussing the diagnosis of the diseases represented in votive pictures of the fourteenth and fifteenth centuries.

The ignis sacer of Celsus was an acute eczema; that of Virgil and Columella, probably malignant pustule (anthrax). Pliny, being a closer observer, describes several kinds of ignis sacer. Later writers took the name variously to signify malignant pustule, scarlatina, scurvy (Bateman), and so on. Ehlers says that to Thuillier belongs the honour of first detecting the part played by ergot in the tragedy.

The first epidemy which can with some certainty be ascribed to ergot is recorded in the annals of the convent of Xanten on the Rhine (1). The gangrene of ergot was not always dry; it is here stated that "detestabili eos putredine consumpsit, ita ut membra dissoluta ante mortem deciderent." A hundred years later the people of Paris were flocking into the churches to pray for cure of their sufferings from ergotism.

In the same (tenth) century 40,000 persons are said to have died of the "feu sacré" in Aquitaine, Limousin, and neighbouring parts. "The cries of the sufferers were piteous; the stench of their limbs was intolerable; and many were carried off in a night." The only persons to come well out of the affair were the clergy, who received rich donations. The bishops of Aquitaine carried the relics of St. Martial in procession; when, indeed, as if by enchantment, the plague ceased. Ehlers maliciously suggests that the procession took place in the late spring, at which season the poison becomes attenuated. But it ceased after terrible affliction: "his temporibus pestilentiae ignis super Lemovicines exarsit: corpora enim virorum et mulierum supra numerum invisibili igne depascebantur et ubique planctus terram replebat." The scourge was most virulent in the end of the eleventh and early twelfth centuries, at the time of the Crusades. The harvests were bad and the bread discoloured. Dauphiné was so smitten that Pope Urban the Second founded a religious order at Vienne devoted to St. Anthony; an order to bring help to the afflicted. There were several hospitals of the order in France. That at Lyons, as Rabelais tells us, had its doors painted red, emblematical of the fire. Germany, Flanders, Burgundy, Denmark, and other countries suffered heavily, and even England. Whole districts were depopulated as if by the bubonic plague. The English epidemy is described as "an epidemic erysipelas whereof many died; the parts being black and shrivelled up." The chronicler, Hugh of Fleury, says that the effects of the distemper were to cause languor, lividity of skin, and a consumption of the flesh, which separated from the bone and was accompanied with intense pain and burning. But the relief of death came not—not until the very vital organs themselves were invaded. Strange to say, the patients were penetrated by an icy chill beyond all warming; and yet the fire burned in the cancered (gangrenous) parts. The saints alone were appealed to; medicine was helpless. "Multa loca mirabiliter pervadit, sed mirabilius per sanctam Dei genetricem Mariam extinguitur."

Hugh of Lincoln is said by his chronicler to have seen many who had recovered from the fire, at Mont-St.-Antoine in Dauphiné. Horribly crippled, their health was nevertheless thoroughly restored; the cripples were of all ages, some lacked a forearm, others a leg, or even leg and thigh up to the groin: all these stumps were soundly healed. To follow this woeful story through the thirteenth, fourteenth and fifteenth centuries would be but to repeat the same piteous tale of poor and ignorant people, the sport of a malignant fate which a word of warning would have averted had there been any to utter it. The result was devastation, physical, moral and civil. Even the saints were apathetic: century after century they abandoned their devotees to appalling mutilations and tortures. It is almost a relief to read that the "mortifer ardor consumpsit multos tam de magnatibus quam de mediocribus atque infimis populi." We hear always the same description, "membris sacro igne exesis, ad instar carbonum nigrescentibus." It was in 1109 that "the people all over England were afflicted . . . by an epidemic erysipelas whereof many died; the parts being black and shrivelled up." Germany suffered in the same way. The "invisible chess-player" pitilessly played on. There is a grim humour in the story that the priests and sextons often suffered much, as the folk would pay the tithe in the lightest grain.

The evil was most destructive in bad harvests and famine; but after the middle of the thirteenth century we hear less of the sacred fire, although it lingered long in the current speech. Dr. Ehlers quotes an instance from Luther, "wie die trewen erzte thun, wenn das heilige feir in die bein komen ist." The plague, however, if less virulent was by no means stayed, as we shall see presently; and the medicine books still contained elaborate recipes for its cure. In the eighteenth century there was an epidemy in Denmark (Holstein) and also in Norway.

Slowly science did for these miserable peoples what the saints failed to do. The Abbé Tessier formed a good judgment of the conditions likely to promote an outbreak (he speaks of La Sologne): I quote three of them—(i.) That the district was damp and foggy; (ii.) That the vegetable products were ill-thriven and stunted; (iii.) That the inhabitants were in bad health, being reduced by want and malaria.

Thuillier now discovered that the cause of the plague lay in the spurred rye; that the intensity of the malady is in proportion to the dose of this poison; and that the rye is spurred in damp and cold seasons. Experiments performed on animals corroborated the other evidence, after the manner of Koch.

M. Dodart, in the year 1676, was commissioned to investigate the nature of the disease; and in addition to previous observations he discovered that the ergot is most active when it is new, and loses much of its virulence as it grows stale. He describes the symptoms with some care and accuracy; to these, however, we shall return hereafter. C. N. Lange, says Ehlers, gave an admirable account of an epidemy of ergotism in the cantons of Berne, Lucerne and Zurich, in 1709. He speaks of the excruciating pain which preceded and accompanied the gangrene; in many cases and epidemies pain was absent, but it was usually a terrible feature of the mediæval ergotic plague. In other of Lange's cases the symptoms were rather a heaviness of the head and stupefaction, followed by a kind of drunkenness; this series was especially seen in those who ate their bread hot. The like observation of the more deadly effects of hot ergotised bread appears in other histories. Lange also traces the pest to ergot in a very careful way. This epidemic spread in Dauphiné and Languedoc; and we have a full account of it in the archives of the Abbaye St. Antoine at Vienne. The ruthless persistence of the malady is again noted, the victims often being in torture for six months or more before the release of death. The physician of the abbey also notes the devouring fire which burns the affected parts, cold as they appear, with intolerable pains. He describes the gangrene as of the black and dry variety; but another doctor of the abbey saw many cases in which the gangrene was not altogether dry, but, suppurating, stank horribly and was filled with worms. Four hundred parishes in this part of France were attacked—men, women, and children indiscriminately.

In 1746-47 there was a terrible outbreak in Sweden, Russia, Sologne again, les Landes, Artois, Flanders, and other places. In this epidemy pain was most violent; so that the fire in the limbs drove the victims hither and thither—some in their agony hurling themselves against the walls or even into the water. Those grievously attacked generally died; those who survived became blind, dumb, or demented. Salerne proved the poison on pigs, ducks, and fowls; and the animals died of gangrene. He corroborated the statement that the fresh ergot was the most virulent, and that after some months it sweated and lost its poisonous properties. About this time Linnæus led observers into error by alleging that the malady was due to the radish (raphanus); and thus his authority led to the name of raphania for ergotism. It does not appear that Linnæus had ever visited the ravaged districts; and it has since been shown that the raphanus is never poisonous. Later in the eighteenth century there were many severe outbreaks in many parts of Europe; one of them (small in extent) in Suffolk. An observer in one afflicted district found an average of twenty spurred grains in each handful. Wagner (34) reported one-fifth of a bulk of rye to be spurred; and Bruce says that 10 per cent of the meal might consist of ergot.

Ergotism has by no means ceased in Europe: it is, however, almost confined to the Russian Empire, in many parts of which it seems to be still endemic. Speaking generally, a better knowledge of the causes of the disease and of its treatment has lightened the weight of the plague. Still many and grave cases are seen; and during this century many epidemics in many parts of Europe have been described. The year 1845 seems to have been very fertile in ergotism: in 1881 there was a great outbreak in Ekaterinoslav; and in 1883 a like outbreak occurred in Tomsk—out of 300 patients 36 died. As is well known, Professor Kobert of Dorpat has studied some of the Russian epidemics, and has analysed the ergot with a view of determining its active constituents. Kobert tells us that ergot contains two poisons: sphacelinic acid, which provokes the gangrene; and cornutine, which causes the anæsthetic and convulsive ergotism—to which the German name of Kriebelkrankheit is more particularly applied. By the predominance of the one poisonous element or the other the varieties of the pest are explained: the ergot of rye of France contains more sphacelinic acid; the German "Mutterkorn" is richer in cornutine. Dr. Ehlers thinks this explanation too neat to be true. I see that Dr. Lauder Brunton repeats Kobert's statements without expressing an opinion on their accuracy.

To avoid detaining the reader by a description of the most recent and therefore most scientifically described epidemics, I shall now content myself by giving, in the list of references, the titles of the most important of the reports and studies of recent years. For these references I am largely indebted to Dr. Ehlers' excellent bibliography.

Causation.—Ergotism properly falls under the head of bacterial diseases; for its immediate cause is the poison of a microbe, the Claviceps purpurea, and perhaps of the common corn-smut (Brunton); remoter causes are starvation, misery, and ill-health. Moreover, it appears that, in the case of ergot as of most other poisons, there is a peculiar susceptibility to its effects in certain persons; so that severe poisoning has followed the use of ergot even in medicinal doses: in some rare cases, indeed, after a single large dose (Robert). Another example of this susceptibility will be mentioned in the article on "Diabetes insipidus" in the next volume of this *System*. Often in epidemics of ergotism some members of a stricken family escape; other patients are sporadically victims in the midst of general immunity. Again, those persons must suffer first and chiefly who are mainly or altogether dependent on the diseased corn for food. Thus cattle died first in some epidemics; and those labourers whose food was but bread and water. So long as milk, cheese, or meat formed part of the diet the peasant suffered less severely or not at all. The proprietor who dressed his own corn was better protected than the workmen who had to take their corn from the miller, who bought the cheapest grain he could get. Age and sex are indifferent factors, but Dr. Bruce says the disease is unknown in children at the breast. In stricken houses the misery must have been indescribable! Children lying on the earthen floor writhing in convulsions, others crying for hunger, all lacking clothes to cover their nakedness; the wretched parents, crippled perhaps by gangrene, unable to relieve their children's sufferings or to avert their own. Well may we exclaim "quæ lucis miseris tam dira cupido!"

Symptoms.—Ergot may prove fatal by acute intoxication or by slow torture. It may occur in two chief forms at least, the spasmodic or convulsive, and the gangrenous—the variation being probably due to the variable quantities of two or more poisonous principles in the spur. In the acute form, which is more common in children, heaviness of the head, giddiness, depression of spirits, and formications may pass rapidly into colic, tympanites, clonic and tonic cramps (Krummekrankheit), precordial anguish, violent vomitings, purging, and stupor with or without convulsions (epilepsia epidemica): if death ensue in one or two days, as is not infrequent, the seizure is not unlike cholera, but with a more clouded sensorium. A vesicular eruption has been seen in some cases. If convalescence follow an acute attack, which is a rare result, it is very tedious and imperfect, broken by relapses, and dogged in after-time by such sequels as epilepsy, weak-mindedness, cataract (Taube, Meier, Graefe), and many other misfortunes. The gangrenous form may also set in with terrible vehemence, though of course for the destruction of the limbs more time is required. The agonising pain to which I have referred may penetrate the affected limb, or limbs, like a fire; but, on the other hand, there may be no pain. An erysipelatous blush may precede lividity; but usually it is absent, and the lividity passes into darkness or blackness. As a rule the gangrene is dry; but moist gangrene is seen occasionally. An inflammatory band marks off the dead part, which separates without hæmorrhage. More than one limb may well be affected; and part after part, until the body and viscera are involved, and death ends the ruthless course of the disease. At first the blood-pressure is raised: the radial artery is felt to tighten from day to day, and the pulse becomes very small; as the disease advances it becomes almost or quite imperceptible. When the mischief is arrested at an earlier stage, and the poor labourer recovers, he is probably crippled by the loss of hand, foot, or limb.

The malady may pursue a very chronic but not less pitiless form, when all the symptoms invade the body very gradually. The erysipelatous skin may die first and become detached as the slough of a snake.

Again, there may be a mixture of the spasmodic and gangrenous symptoms in the same patient.

In mitigated attacks there may be little more than heaviness of the head, melancholy, some creepings, and slight tonic contractions of the legs; the appetite may not fail, and the paresis may not go beyond anæsthesia. In this stage it is not uncommon for patients to show so much anæsthesia as, for example, to sew a finger to needlework. It is a good sign when the creeping returns; an irritation may follow, annoying enough, but welcome, as in recovery from frost-bite; heat returns to the cold limb, and the characteristic pallor of the face gives place to a freshening tint. These recoveries are more common in the spring and early summer before the new grain comes into use, and as the old spurs are losing their virulence.

Diagnosis.—Ergotism, only too easily recognised in times of epidemic, may not readily be detected in sporadic and mitigated cases.

Dr. Ehlers does not hesitate to raise the whole question of the relation of other diseases marked by ischæmia of the extremities to ergotism; such as acrodynia, Raynaud's disease, and erythro-melalgia. As to acrodynia, Ehlers unhesitatingly attributes the cases described by Rayer to ergot. The disease arose spontaneously, appeared epidemically, and in damp seasons. The symptoms certainly presented the characters of ergotism. As to Raynaud's disease, Ehlers submits Raynaud's cases to a very careful scrutiny, with the effect, in my opinion, of establishing a case for renewed criticism of my late friend's work from the present point of view. Ehlers alleges that ergotism and Raynaud's disease arise at the same season; that Raynaud was mistaken in supposing that ergotism respects certain ages or one sex; and, finally, that the cases Nos. 9, 12, and 15 of Raynaud were certainly ergotism. No. 9 and No. 12 were in patients who ate rye habitually. In the young woman, No. 15, a gramme and a half of ergot had been administered in her confinement three days before the symptoms began. Robert relates a case in which sixty centigrammes of ergot caused gangrene in a woman shortly after confinement, and death a month later. In other cases Ehlers hints that young women may forget to inform their medical adviser that they have been taking ergot, even if they were aware of the contents of some medicine taken for abortion. Other cases, he thinks, were too indefinite in character to permit of an accurate diagnosis. I must add, however, from personal knowledge as well as from the evidence of his treatise, that Raynaud did not overlook the possibility of ergotism in his cases and decided against this poison.

In 1872, and again in 1878, Dr. Weir Mitchell described a group of symptoms under the name of erythro-melalgia, and reported six cases. Many cases have subsequently been put on record. One of these, recorded by Nieden, is pronounced by Ehlers without hesitation to be one of ergotism: he is disposed to put the same interpretation on others of these, and urges that all these cases should in future be studied in the light of ergotism. The superficial resemblance of acute ergotism to cholera has already been mentioned. Confusion between the two maladies is not likely to arise.

Prognosis.—The mortality in severe epidemics may be as high as 60 per cent; in the less severe it may fall as low as 10 per cent. As I have said in another section, the symptoms of gangrene may pass off and the limb recover; but this event is not to be anticipated. Acute ergotism is generally fatal. In chronic cases much depends on the dose of the poison and on the subsequent prevention.

Pathology.—The sensory nerves are paralysed, but it is uncertain whether the action be central or peripheral (Brunton). The muscles and motor nerves are unaffected. Dr. Bruce says that the posterior columns of the cord are the seat of a sclerosis somewhat resembling that of tabes dorsalis. The heart is not so obviously affected as the arteries. The arteries are thrown into a state of contraction, producing a rise of blood-pressure. In some measure, however, this rise is due to stimulation of the vaso-motor centre in the bulb. It is said that in the constricted and thrombosed arterioles a glutinous matter (decolorised plasm ?) is found, and the walls of the vessels either primarily or secondarily undergo a hyaline degeneration, especially of the tunica intima. The blood drawn during life is dark and viscous. By the contraction of the intestines and other viscera also the blood-pressure is raised. After death the abdominal viscera are found "inflamed" (Brunton). Ehlers repeats the serious warning, therefore, against the use of ergot in enteric fever, in which disease it may do fatal mischief.

It is generally stated that respiration is slowed from the beginning, and that death is due to palsy of the respiratory centre; but Dr. Bruce says that the respiration is unaffected. The uterus, intestines, and bladder are tetanically contracted, and this author strongly disapproves of the continuous medicinal use of ergot as apt to do grave harm.

The attribution of these several phenomena to the respective constituents of the spur is not yet possible.

There are no specific means of treatment; or none is known as yet.

The detection of ergot in flour is thus performed:—a small quantity of the sample is mixed with ether, and a few crystals of oxalic acid are added; if the liquid, after being boiled and allowed to become clear, exhibits a red tinge, ergot is present in the sample (Böttger).

B. PELLAGRA is a disease which presents many analogies to ergotism. Indeed the nature of the poison seems to have a nearer relation to that of ergotism than one of mere analogy. Like ergotism, and a few other diseases, it is the effect of a toxine which falls rather upon the nervous system, but manifests some of the most characteristic of its effects at the periphery.

Pellagra is at times epidemic in its invasion; at other times or places it is endemic or sporadic. The best account of the plague which has come into my hands is that of Tuczek. Tuczek sums up the work of his predecessors; and his own observations seem also to have been very extensive; he visited all the chief lunatic asylums in North Italy, where unhappily the wrecks of this affliction are everywhere to be found. It is in these asylums that I have obtained the very small amount of experience of pellagra which I can call my own. The pestilence is very prevalent in Roumania; in 1888, 10,626 persons in Roumania, out of a total population of 5,339,650, were suffering from pellagra. It is well known to prevail also in the south of France and north of Spain. Since 1856 the disease has shown itself in Corfu. The first accounts of pellagra came from Spain. Casal in 1762 described the disease in the Asturias under the name of *mal de la rosa* (Creighton): the Asturias are still its headquarters in Spain. In Italy, Dr. Creighton tells us that it first broke out in the neighbourhood of Lago Maggiore; and in 1750 it rapidly extended its ravages in North Italy. Its extension in the Emilia and in Tuscany has taken place during the present century. In Central Italy it is little known; in South Italy and Sicily it is not seen at all. Like ergotism, pellagra is a disease of the poor, especially of the poorest.

The Italian peasantry are for the most part in a wretched condition; they are ill clad, ill fed, oppressed by hard labour, and housed in huts scarcely fit for the domestic animals.

Causation.—Although pellagra, like ergotism, is associated with bad food and water, misery, and grinding labour, yet these conditions, which favour the disease, are not sufficient of themselves to produce it: the peasantry in Southern Italy are even more miserable than those of Lombardy. A more specific cause is necessary; and there is now no doubt that this immediate cause has been traced to bad maize. It would seem that pellagra is not so definitely a microbic disease as is ergotism, but belongs rather to the class of food poisonings; strictly, perhaps, it should have found a place in a subsection of ptomaine poisoning. The toxic body or bodies have not yet been separated. Dr. Creighton points out that although maize forms a large part of the staple diet of the peasantry in other countries than those subject to this plague, yet beyond its ordinary haunts pellagra does not occur. "Compared with the maize zone the area of pellagra is a mere spot on the map." Even in countries such as Burgundy, Franche Comté, and the Bresse, where the climate and soil are somewhat trying for maize, pellagra does not appear; in these provinces the greatest care is taken to dry the grain before it is stored, yet after a particularly bad harvest pellagra may arise. These considerations make it very improbable that, as De Giaxa insists, sound maize may set up the disease in susceptible persons.

Pellagra is less prevalent where the maize is supplemented by other foods. Corfu, as Dr. Creighton points out, is almost a crucial instance: maize thrives well there, but its culture has been largely displaced by vine culture; since this change maize has been imported, and the importations consist of the inferior maize of Roumania still more deteriorated during a long water transit by the Danube and Black Sea. The Wallack peasantry of Roumania, who are subject to pellagra, gather the corn before it is ripe, and shoot it into pits, where it becomes musty. In Northern Italy the peasantry grow the more worthless kinds of maize on poorly cultivated grounds, sow it late, harvest it before its maturity, and carelessly store it undried. The millers grind the cheapest corn for the peasants' use; moreover, the loaves are unleavened, half-baked, and turn mouldy before they are consumed. This kind of evidence goes no farther than to indicate that the poison is due to ordinary putrefactive changes—changes due, no doubt, to microbes; but the microbes concerned may be the ordinary agents of decomposition: the special characters of maize poisoning may be due to some peculiarity in the chemical structure of this grain itself. The cryptogam to which the disease is provisionally attributed is the Reticularia ustilago; its spores are seen as a brown or greenish brown powder which is deposited under the epidermis. This fungus is found in other diseased grain, yet in the case of maize only is its invasion followed by the pellagra. There seems, therefore, to be some quality in the maize itself which, when acted upon by the "verdet," as the fungus is called, produces a specific poison. It may be, of course, that the "verdet" has nothing to do with the disease, and that some other parasite has yet to be discovered in the musty Indian corn.

Pellagra is chiefly a disease of middle life, and of women more often than men; but children are attacked not infrequently, and Creighton, treating of its heredity, says that infants at the breast may show signs of it: he adds, however, that such infants are partly fed on the household polenta.

Symptoms.—Pellagra stamps its most signal feature upon the skin; hence it is often thrown into the heterogeneous class of skin diseases. But on careful observation it will be found that the eruption is usually, if not always, preceded by constitutional disturbance; of which the first symptoms are headache, depression of spirits, sleeplessness, paræsthesias, cramps, palsies, vague but often severe pains in the spine and joints, vertigo and dyspepsia. In the later stages diarrhœa sets in. The dyspepsia, in my judgment, seems to be the first disorder to follow the invasion of the poison. Agostini, who has made a careful investigation of this part of the disease, says that there is a marked degree of "hypopepsy" due to catarrh; while motor and glandular insufficiency are well marked. In severe cases free hydrochloric acid may be altogether absent; in all it is much reduced. Digestion is therefore slow and imperfect; peptones are deficient, and the catarrhal discharge facilitates the lactic and other fermentations. Agostini states that careful attention to this stomach derangement, including lavage, is of benefit in pellagra. To expect a means of diagnosis from analysis of the stomach contents seems unsatisfactory; by the time these changes assume any characteristic degree —if they are ever characteristic—the diagnosis would probably be assured on other grounds. As the malady progresses the skin disease appears, though the eruption is not constant; there may be "pellagra sine pellagra." The eruption nearly always appears in the spring, and its recrudescences occur chiefly in spring; it is not clear that this preference depends on any seasonal activity of the maize poison, and it seems more probable that it is due to the increasing power of the sun upon the surface of the body.

The eruption, as described by Mr. Malcolm Morris, is an erythema which chiefly affects the parts exposed to the sun. The skin is swollen and tense, and is the seat of burning or itching sensations; petechiæ are frequent, and bullæ appear, which on rupturing leave indolent ulcers (pellis agria = ulcer of the skin).

In about a fortnight from the beginning of the attack the erythema subsides, and desquamation follows, leaving the underlying skin thickened and stained of a light sepia colour. The symptoms usually subside in the autumn, to reappear, however, in the following spring. The attacks thus recur regularly every year, the thickening and pigmentation being increased on each occasion in the first four or five years. Afterwards the integument undergoes atrophy, and becomes dry and wizened as in old age: this atrophy is especially marked on the backs of the hands. The nails and hair show no change.

When the patient has thus been the subject of the disease in its recurring attacks for three or four years his depression of spirits deepens into melancholia of a severe and irremediable kind. He commonly suffers from globus. The melancholia may be altogether dull and heavy, or on the other hand it may have maniacal phases: the patient may be moody, self-accusing, and remorseful, or he may present maniacal periods, in which misery or a horrible burning of the skin may drive him to suicide. Systematic monomania ("paranoia") is never seen. As depression may alternate with mania, so stupor may alternate with the vertigo; and twitchings, tremors, and even epileptiform seizures of the cortical variety are not uncommon. The cramps, likewise, may pass on into permanent contractures.

Palsies form part of the ordinary course of the disease; the knee-jerk may differ on the two sides; but in the large majority of cases it is increased: it is rarely absent. Tendon reflexes are often to be detected in the forearms. The gait, though uncertain, is never ataxic; it rather assumes the form of spastic paraplegia. Ankle clonus, though often present, is not invariable. These paretic symptoms are commonly preceded by tremor. Sensation is virtually unaffected.

Together with this degeneration on the side of the nervous system the whole man also deteriorates. Flesh and strength fall away, the mental faculties wane, and life is but too often prolonged to the dregs, to be cut short at last by colliquative diarrhœa. With each successive year, to use Dr. Creighton's words, the patient becomes more like a mummy; his skin is shrivelled and sallow, or even black at certain points; his bones protrude; his muscles waste; his movements are slow and languid, and his sensibilities grow more and more obtuse.

Pathology.—Whatever the poison, its effects, as in the case of ergotism and lathyrism, fall directly upon the nervous system; and the main external features, such as erythema and gangrene, are secondary to degenerations of the nervous structures, whether of vaso-motor or directly "trophic" origin. Although the vaso-motor changes are not so definite as in ergotism, yet in pellagra they seem to be of no small account. The most obvious changes are found, however, in the spinal cord; and these are precisely such as the palsies would lead us to expect. Both in ergotism and in pellagra the posterior columns are injured, but with a difference. In the most painful cases of ergotism the posterior root-zones are attacked; in pellagra, as the preceding report of the symptoms would indicate, the lateral columns rather are implicated. On post-mortem examination it is found that although the posterior columns do not escape, the median portion being often degenerated, the posterior root-zones are never attacked. But the weight of the disease falls on the crossed pyramidal tracts. The direct cerebellar tracts are never touched. The cells in the anterior horn are deeply pigmented; but the muscular atrophy of the later phases of the malady is general, not particular. The lesions of the posterior columns fall chiefly upon the cervical and upper dorsal region: those of the lateral column rather upon the middle and lower thirds of the dorsal region. Pigmentation is also found in other internal organs and in the skin. In pathological character the changes seem rather to be extremely slow degenerations than inflammations: they are probably not essentially of a progressive kind; the advance of the mischief, at any rate in the earlier stages of the disease, depends on the persistence of the cause. The brain presents general wasting; the ventricles are somewhat distended and contain some excess of fluid.

Diagnosis.—In countries where pellagra is known there can be little difficulty in detection of the malady, even in its early stages. The only diseases to which it shows any likeness belong to the same class of progressive dementias. General paralysis of the insane might at certain moments present some resemblance to pellagra; but the character of the lesions of the limbs or, if in rare cases these be absent, the lack of grandiose ideas, the features of the palsy, and the history of the origin of the attack, would direct the observer to a true opinion. The speech may be affected in pellagra, but not in a characteristic fashion. The pupils are never fixed as in tabes, but some myosis is often present. Cases are, however, recorded of the coincidence of the two maladies in the same person. The disturbances of sensibility, if any be present, and the eruption may suggest leprosy; and leprosy, like pellagra, may present remissions if not definite seasonal phases. In nodular leprosy, however, the granuloma of the skin, and in anæsthetic leprosy the nerve changes, are characteristic. The colour of the skin may not be unlike that in Addison's disease; but the eruption, or in its absence the nervous symptoms of pellagra, would suffice to indicate this disease.

Prognosis.—When the disease has recurred for three or four seasons, and especially if the mind be affected, the prognosis is very bad. I gathered from the physicians of the Italian lunatic asylums that recovery of patients once arrived at the asylum stage of insanity is almost unknown. Still these are extreme cases; the mentally afflicted in their earlier phases may recover: only too often, however, the advance of death is inexorable.

The only treatment is to remove the causes of the intoxication, and of the failure of resistance, and thereafter to treat the symptoms on general principles.

The Ministry of Agriculture in Italy has provided drying apparatus for grain, bakeries, and other hygienic advantages, including better house accommodation, in the infected districts; also "pellagrosari," or places for the treatment of "pellagrosi," for those patients on whom the disease has gained a hold. It is stated (37*a*) that a decrease of the malady has followed on these reforms; except in the district of Perugia, in which, for certain incidental reasons, the malady seems to have increased.

C. LATHYRISM is the name given by Cantani to another *mal de misère* due directly to diseased grain, and more remotely to wretched conditions of life. At the end of the last century, and at the beginning of this, suspicions arose that certain palsies of the legs were due to the use, as food, of the Lathyrus sativus and the L. cicera (or chick pea). The disease has been observed in the departments of Loire et Cher, in the Abruzzi, at Alatri, at Allahabad, and in Kabylia. No poisonous substance has been separated from the pulse; and indeed the precise species concerned is not finally determined. It is said that foreign seeds, such as a species of Ervum, mixed accidentally with the pulse, may do the mischief; or again that the L. purpureus or the L. clymenum may be the offending ingredient. On the whole it seems most likely that the L. sativus or cicera, or both, are concerned in the evil. An exclusive or almost exclusive diet on the chick pea, and wretched conditions of life, seem, as in the two preceding diseases, to be accessory causes. The outbreak at Allahabad, described by Irving, followed a failure of the wheat crop.

Symptoms.—Lathyrism is a quicker disease than either of the two preceding, and not so ruthless. One morning the patient may find himself unable to get out of bed; his limbs are stiff and creepy, and in some epidemics much pain in the back is complained of. During the next few days a tremor and uncertainty are observed in the hands, and the stiffness of the legs is seen in a peculiar gait which differs somewhat from that of ordinary spastic palsy. The accounts which I have read seem to describe a peculiar rigidity of the dorso-lumbar muscles set up on the side opposite to each leg as it is advanced in turn; giving, if I understand the account properly, a throw of the trunk backwards and sideways against the weight of the advancing leg. Thus, as the patient walks, the head and body must be thrown into a succession of curves, describing a screw or a chain of figures of eight. The leg, on the other hand, with the toe pointed and the heel drawn up, is thrust out with a tremulous extension and adduction; thus the toe reaches the ground before the heel, or the heel may never reach the ground at all, and the gait become a tripping on the toes. In some epidemics the gait is said to have more of an ataxic character, and the pain to be greater; as if the poison fell more on the posterior columns.

The disturbances of sensation seem to be no less remarkable. Hyperæsthesia and paræsthesia of the legs may be followed by anæsthesia, when the skin reflexes are lost. The tendon reflexes, however, are intensified, as the reader will surmise. Intolerable creepings, as in ergotism, also torment the sufferer. The application of the hot moist sponge to the spine calls forth this creeping and tremors of the legs.

The evolution of these various symptoms takes four or five weeks. The sphincters are not affected as a rule; but in severe epidemics and in bad cases both anal and vesical sphincters are said to be palsied. Retention of urine is more common. Sexual power is enfeebled or lost. In none of the accounts which I have read is mention made of the arms, save as being occasionally tremulous; it would seem, then, that the poison falls rather upon the lower part of the cord.

Pathology.—Lathyrism is a milder disease than either of the preceding kinds of grain poisoning; hence no doubt the great imperfection of the post-mortem records. Such notes as "softening of the cord," and other such inaccurate and vague phrases, give us little information; at present, therefore, the precise lesions can be inferred from the symptoms only. These, I need scarcely say, point to the lateral and posterior columns in the lumbar region as especially the seat of the activity of the morbific agent, whatever this may be.

Diagnosis. — The only disease which simulates lathyrism at all closely, is Erb's syphilitic spinal palsy. The epidemic occurrence of lathyrism and probably the absence of all syphilitic antecedents will suffice for distinction. In case of doubt the grain may be tested on animals.

Prognosis seems to be more favourable than in the two former kinds of grain poisoning. If the diet be changed before the cord has become deeply disorganised, recovery, as I understand, is to be anticipated.

Treatment at present consists only in this change of diet and in reform of other adverse conditions of life.

Domestic animals seem to be liable to lathyrism; though on this matter, again, there seems to be some difference of opinion. Some authors assert that animals have been fed in vain on the pulse, no morbid consequences having followed. In other epidemics the domestic animals are said to have suffered distinctly enough.

I accidentally dropped upon two descriptions of lathyrism in horses, induced by feeding them on lathyrus, which are of much interest from a pathological point of view (45, 46). The horse seems to present a series of symptoms different from that of man, which may account for the discrepancy of the accounts of the susceptibility of animals. In the horse the heart and respiration are chiefly affected, and the larynx especially; so that the animal stands with stretched-out neck striving against the asphyxia which soon destroys him.

After death the mischief is found mainly in the cells of the anterior horns of the cord, which are diminished in number and atrophied; there is also thrombosis of the small arteries. The arteries are also thickened. The heart presents signs of fatty degeneration, and so likewise do the intrinsic muscles of the larynx.

If on careful repetition of these observations the results are found to be constant, and to be attributable to the pulse, they may indicate that the nervous mischief is not primary, but consequent upon vascular lesions. Thrombosis is mentioned in the accounts of the spinal lesions in man. If this be correct it would suggest a similarity of action between the lathyric and the ergotic poisoning, in the former of which, as we have seen, coagulations are formed in the smaller arteries.

T. C. ALLBUTT.

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T. C. A.

MUSHROOM POISONING

Cases of poisoning by certain funguses, eaten in mistake for the edible mushroom, are far from uncommon. The poisonous element in most of these cases is muscarine. Muscarine has been produced artificially, but the artificial drug seems to differ in some quality from the natural alkaloid (Brunton). Muscarine belongs to a large group of substances, the individuals of which are not yet definitely discriminated; they are closely allied to the substances known as ptomaines [*vide* art. "Ptomaine Poisoning"]. In some funguses choline is the active agent; but choline and muscarine are closely allied bodies. Happily nearly all these bodies tend to produce vomiting, so that the sufferer usually rejects some part of the poison. The diarrhœa likewise, so often a feature of this kind of poisoning, may be eliminative.

Muscarine, choline, and their allies are therefore to be regarded as products of decomposition of nitrogenous substances. Perhaps no mushrooms are safe as food if they be in a state of putrefaction. This is not the place to give a careful account of the characters which distinguish the edible funguses from the poisonous. We cannot absolutely say that every mushroom with pink gills and a ring on the stalk is safe; but this rule is generally true no doubt. No reliance can be placed upon previous preparation or cooking to avoid the dangerous properties of the poisonous kinds.

Symptoms.—Muscarine and its allies are most active poisons. Not long after the meal, vomiting, diarrhœa, prostration, and even cramps set in. By the myotic action of muscarine the vision may be affected. This poison also salivates, though it represses perspiration. The most remarkable effect of muscarine, however, is upon the heart; it paralyses the cardiac muscle and stimulates the inhibitory ganglia. In children convulsions may occur. In fatal cases the internal organs present no characteristic features.

Diagnosis.—If the pupils be contracted, and, again, if bits of fungus can be detected in the vomit or stools, the diagnosis is certain; even if the circumstances of the occurrence be not explicit. In any case the symptoms will point to poisoning by some cadaveric alkaloid.

Prognosis.—Recovery is the rule in these cases, unless the dose be very large and the rejection of the poison very defective. Collapse and failure of the heart and respiration are the chief dangers to be averted.

Treatment.—The first end to be sought is to procure elimination of as much of the offending substance as possible. The emptying of the stomach is to be aided by the usual means. Exhaustion must be combated by diffusible stimulants by the mouth, or, if this be difficult, by the skin. Happily we can do more than this: muscarine has a specific antagonist in atropine. By this physiological antidote the dangerous effects of muscarine upon the heart and respiration are opposed. As soon as the pupils dilate, or sooner if the case be understood, sulphate of atropine must be injected subcutaneously, and the dose repeated as seems necessary. At the same time, of course, other means of restoration will not be forgotten.

T. CLIFFORD ALLBUTT.

SNAKE-POISON AND SNAKE-BITE

VENOMOUS snakes are found almost all over the temperate and tropical regions of the world, with the exception of New Zealand and Oceanic Islands. They are divided by naturalists into two main classes—(i.) poisonous colubrine snakes; (ii.) viperine snakes. These two classes present differences in structure, and also in the properties and toxic action of their poisons.

Among the more important of the poisonous colubrines are the cobras (*Naja*) and kraits (*Bungarus*) in Asia; the coral snakes (*Elaps*) in South America; the moccasins (*Ancistrodon*) in North America; and the tiger snake (*Hoplocephalus curtus*), black snake (*Pseudechis*), and deaf-adder (*Acanthophis*) in Australia.

The Viperidæ are represented in England by the small viper (*Pelias berus*); and some other small species are found on the continent of Europe. North America possesses the rattlesnakes (*Crotalus*); and Asia the chain viper (*Daboia Russellii*) and *Echis carinata.* There is no true viper in Australia.

Poison apparatus and mechanism of bite.—The poison is secreted by the cells of a compound racemose gland, possessing large alveoli which serve as a receptacle for the venom. The glands, one on each side of the head, are placed behind the orbit, and beneath the masseter muscles, with which they are intimately connected. In an adult cobra they are about the size of a large almond. The gland is the homologue of the parotid salivary gland in other vertebrates. From the anterior margin of the gland a duct passes forward along the side of the upper jaw. Just in front of the fang it doubles on itself so as to open by a small papilla on the anterior wall of the sheath of mucous membrane which embraces the base of the tooth.

The fang, in the great majority of venomous snakes, is a functional tube, with the lower opening on the anterior surface near the base, and the upper opening on the same surface within a short distance of the point. The gland duct is composed of fibrous tissue and is lined with epithelium. Numerous small gland alveoli open along its course. Dr. Weir Mitchell found a muscular sphincter in the course of the duct in crotalus; but no muscular tissue has been observed in other species.

When the snake opens its jaws before striking, the poison-fangs are erected, and the sheath of mucous membrane is drawn tightly over the anterior surface of the tooth, so as to bring the poison-duct into apposition with the opening at the base of the fang. Erection of the fangs takes place to a greater or less extent in different snakes, and is effected by a somewhat different mechanism in various species. When the snake strikes it closes its jaws like a dog on the part bitten. The principal muscles which close the jaws are the masseters and internal pterygoids, the former of which is inserted into the capsule of the poison-glands in such a manner as to compress it powerfully when the muscle contracts. Thus the poison is discharged at the moment the fangs penetrate the skin.

Description of venoms.—To obtain venom in a pure state for purposes of chemical examination and experimental inquiry, the best method is to allow the snake to bite an ordinary large watch-glass which has been covered with thin rubber sheeting, such as dentists use. The fangs penetrate the rubber and all contamination by the secretions of the mouth is effectually prevented.

Snake-poison is a clear, limpid fluid of a pale straw to yellow colour. The colour varies with the pigmented habit of the snake, and also with the concentration of the venom. The reaction of the venom is almost invariably acid. The alkalinity observed in some cases may be accounted for by admixture with alkaline saliva. The specific gravity of venoms varies considerably; but on an average it is about the same for most varieties of snakes, namely, 1050. Venoms usually contain about 30 per cent of solids; but I have myself seen variations in the poison of Australian snakes of the same species between 12 per cent and 67 per cent; and Nicholson in cobra venom has recorded variations of nearly as wide a range. Most venoms are tasteless, but cobra poison is said to possess a disagreeable bitter taste.

Venoms dry rapidly at 16° to 20° C. in a desiccator over calcium chloride. As they dry they crack in the same manner as albumin or gum-arabic under the same circumstances, and form translucent scales which have suggested a crystalline structure. Dried venoms dissolve again readily and completely in water. Perfectly dry venom in a well-corked bottle keeps indefinitely. Weir Mitchell kept some crotalus venom in his possession twenty-two years without apparent diminution of toxic power. I have had some venoms for nearly three years which are as deadly at the present time as when first procured. Venoms in solution in water do not keep well; and perhaps the many assertions that dried venom deteriorates with age may be accounted for by imperfect desiccation. Solutions of venom in glycerine keep indefinitely.

Microscopical examination of pure venom reveals nothing except an occasional epithelial cell; but if the poison be contaminated with fluids from the mouth it contains epithelial scales and salivary corpuscles in abundance, and also bacteria of various kinds.

Composition of venoms.—It has long been known that snake venoms contain albuminous bodies in solution; but, owing to ignorance of the toxic properties of proteids, the active principle was sought for in other constituents. Weir Mitchell was the first to demonstrate the fact that the poisonous properties of rattlesnake venom reside in the albuminous constituents; and the work of this accomplished author on the venom of the rattlesnakes formed the first step in our knowledge of toxic proteids. Since Mitchell's work was published his results have been extended by other observers to a number of different kinds of snakes. The possibility that the effects of venoms are due to constituents other han proteids has been carefully considered; there is now no doubt that he active agents in all venoms are proteids. Venoms are almost pure olutions of proteids, and indeed contain little else except a trace f inorganic salts, a small quantity of an organic acid and a colouring matter. Ultimate analyses of cobra poison have been made by Professor Pedlar of Calcutta and by Professor Armstrong; these analyses point o a general resemblance between the composition of this venom and proteids.

Recent researches on the subject show, as was many years ago pointed out by Dr. Mitchell, that venoms are not simple substances, but contain two or more poisonous proteids; and that in the varying proportions of these in venoms from different species of snakes may be found the explanation of the different effects which follow the inoculation of the several poisons. Some of the proteids present in venoms are classified with difficulty in our present system. A classification which is determined (amongst other reactions) by solubility in water or dilute saline solutions, coagulation by heat, and solubility or insolubility in water or saline solutions after prolonged sojourn under alcohol, is a very arbitrary one; and it is to be expected that, as our knowledge of proteids increases, more individuals of the group will be found which refuse to fall into line with the members hitherto known. The toxic proteids of the poison of pseudechis are completely precipitated by absolute alcohol in excess; yet after six months under alcohol these proteids dissolve readily and entirely in dilute saline solutions. This poison, nevertheless, contains a body which, by its solubility in water and coagulation by heat, would lead one to class it with albumins. The solution of the alcoholic precipitate also coagulates on heating. Weir Mitchell found that the proteids of crotalus venom were completely precipitated by alcohol, and that the precipitate was "more or less soluble in water," "sometimes completely so"; also that its solution coagulated by heat and behaved generally just as the original solution of venom. Cobra venom behaves in the same way.

Venoms contain proteids which possess on the one hand characteristics of the albumins or globulins, and on the other those of proteoses. This has led to a certain amount of confusion—one observer classifying a venom proteid with the albumins or globulins because of its behaviour when heated in solution; another preferring to place the same proteid amongst the albumoses on account of its continued solubility in water or dilute saline solutions after prolonged sojourn under alcohol.

TABLE.—Behaviour of Venoms with Reagents.

	Cobra Venom.	Pseudechis Venom.	Crotalus Venom.
Nitric acid . .	Precipitate; solution on heating reappearing on cooling.	Precipitate; solution on heating reappearing on cooling.	ppt.
Picric acid . .	do.	do.	...
Millon's reagent .	Usual proteid reaction.	Usual proteid reaction.	Usual proteid reaction.
Caustic potash and trace of copper sulphate.	Pink biuret reaction.	Pink biuret reaction.	Pink reaction.
Saturation with chloride of sodium.	ppt.	ppt.	ppt.
Saturation with sulphate of magnesia.	ppt.	ppt.	ppt.
Saturation with sulphate of ammonia.	ppt.; filtrate proteid free.	ppt.; filtrate proteid free.	...
Dropping fresh venom into excess of water.	Slight cloud.	Cloud.	Considerable cloud.
Dialysis . .	Small ppt.; filtrate contains proteid.	ppt.; filtrate contains proteid.	Considerable ppt.; filtrate contains proteid.
5% solution of sulphide of copper.	ppt.	ppt.	ppt.
Alcohol (absolute)	ppt.; solution in H_2O.	ppt.; solution in dilute saline solution.	ppt.; solution in dilute saline solution.
Ferrocyanide of potassium and acetic acid.	ppt.	ppt.	ppt.
Boiling solution .	ppt.; solution still contains toxic proteid in large amount.	ppt.; solution still contains toxic proteid.	ppt.; solution still contains toxic proteid in small amount.

Dialysis throws down all the coagulable proteids of crotalus venom. Some toxic proteid slowly dialyses through. This is especially the case with cobra venom.

From the above reactions it is obvious that all these venoms contain—

(*a*) A proteid coagulated by heat. (*b*) Proteid or proteids not thrown out of solution by this means.

A solution of fresh venom, if acid, gives no precipitate by careful neutralisation with dilute potash, thus excluding albuminate; and after saturation with Am_2SO_4 the filtrate is proteid free, so that no peptone in the present restricted sense of the term is present.[1] The proteids remaining in solution subsequent to boiling are albumoses. Cobra poison contains proto albumose, and so does pseudechis poison. Crotalus venom would appear to contain a body which is more accurately placed amongst the deutero-albumoses.

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[1] Weir Mitchell and Reichert described a "peptone" in crotalus venom. By its reaction this proteid would at the present time be classed amongst the albumoses.

The amount of proteid coagulated by heat varies considerably in the several poisons from different species of snakes. This variation in amount is illustrated by the following table from Weir Mitchell and Reichert:—

	Crotalus.	Ancistrodon.	Cobra.
Coagulable proteid	24·6	7·8	1·75
Non-coagulable proteid . .	75·4	92·2	98·25

The best nomenclature to apply to these coagulable proteids must remain more or less a question of individual opinion. From their retaining their solubility after prolonged sojourn under alcohol, to which treatment globulins are very sensitive, together with the fact that they require nearly complete saturation with neutral salts to precipitate them from their solutions, they may perhaps be better regarded as albumoses than as globulins.

The venom proteids separated by such means as precipitation by alcohol, neutral salts or dialysis, possess all the toxic properties of the original solutions.

Effect of temperature on venoms.—Venoms are not affected by freezing. The effects of heat vary in degree according to the venom operated upon. On the whole they are analogous to the results obtained by Sidney Martin with the toxic albumoses of abrus, and also with the similar proteids resulting from the metabolism of anthrax bacilli.

Heat affects venoms in two ways: (i.) By coagulating some of the proteids present, in which condition they are inert. (ii.) By impairing the toxic power of the proteids present without influencing their solubilities, or indeed changing them in any way recognisable by chemical tests.

The first method of action is sudden. When the solution is raised to a certain temperature some portion of the proteid constituents is coagulated.

The temperature at which this coagulation occurs in some different venoms is for

Crotalus.	Cobra.	Daboia.	Pseudechis.
60°-70° C.	70°-80° C.	70°-80° C.	85° C.

The second method is gradual; the longer the heating and the greater the dilution of the solution, the more impairment of virulence occurs.

Perfectly dry venoms may be submitted to a temperature above 100° C. without diminishing their toxic power. Viperine poisons are very sensitive to heat when in solution. Mere heating to 65° impairs the power of crotalus poison, and a temperature of 75°-80° C. profoundly modifies all these venoms. Some toxic power still remains, but much larger doses are required to produce a fatal result, and the characteristic effects of viperine poisoning have disappeared; the train of symptoms produced becomes more comparable to that of cobra poisoning.

The effect of heat on pseudechis poison is similar. At 85° C. a proteid is precipitated, and the venom has now lost its power of producing hæmorrhagic extravasation, and intravascular clotting; but it still destroys life.

The effects of various reagents on the toxic properties of venoms.—Reagents which precipitate proteids in an insoluble form, or destroy them—such as platinum or gold chloride, silver nitrate, nitric acid in excess, or permanganate of potash—render venoms inert. Solutions of the hypochlorites have the same effect. Carbolic acid if allowed to remain in contact with dilute venom for twenty-four hours destroys its virulence. Prolonged action (forty-eight hours) of caustic potash or soda also destroys venoms.

Gastric digestion does not affect cobra venom nor pseudechis venom. Mitchell states that gastric digestion destroys the power of crotalus venom. Fontana found the poison of the European viper to be unaffected by this means. All venoms are destroyed by pancreatic digestion.

The conclusion that albumoses are the active agents in snake-poisons is interesting when compared with similar results, obtained by Sidney Martin, Hunter, Hankin, Cruickshank and Herroun with the poisons produced by the bacilli of anthrax, diphtheria, and tubercle. Albumoses are the products of the hydration of albumins, and this hydration can be accomplished in many ways; for instance, by boiling solutions of albumin at high pressure, by gastric or pancreatic digestion, or by the vital activity, direct or indirect, of cells. In the case of gastric or pancreatic digestion the result is brought about in an indirect manner; that is, the gland cells manufacture a ferment—pepsin or trypsin—which, under suitable conditions, hydrates the albumins, forming albumoses, and so forth. In the case of digestion by the diphtheria bacillus, Sidney Martin has shown that the bacilli, grown either in the juices of the body or in culture-media outside it, produce by their activity a ferment which is capable of forming albumoses from the proteids. The albumoses formed by such bacilli are highly poisonous, much more so than those produced during gastric digestion, and give rise to the pathological conditions which we recognise as the disease diphtheria. Anthrax bacilli do not give rise to any ferment, but are capable of directly digesting albumins, producing different but still poisonous albumoses. The same is the case with tubercle bacilli.

In all these processes of hydration some of the albumin is further broken up, giving rise to some nitrogenous body of the ammonia type.

In the case of gastric digestion we have a ptomaine pepto-toxin; in pancreatic digestion we have leucin and tyrosin; in anthrax and tubercle digestion we have an alkaloid. In diphtheria no alkaloid is formed, but an organic acid; and the question whether this be nitrogenous is as yet undetermined.

The following table, taken with some alteration from Sidney Martin's Goulstonian Lectures to the Royal College of Physicians, London, in 1892, illustrates this analogy; to it I have added for comparison the results with snake-poison.

TABLE illustrating the Analogy between various Processes of Hydration due to Vital Activity.

Primary Agent.	Ferment.	Products.	
		Albuminous.	Nitrogenous.
Epithelial cell of gland (stomach)	Pepsin	Hetero-, proto-, and deutero - albumoses, peptone.	Pepto - toxin (in artificial digestion).
Epithelial cell of gland (pancreas)	Trypsin	Globulin-like body, peptone.	Leucin, tyrosin.
Bacillus anthracis . . .	(None)	Hetero-, proto-, and deutero - albumoses, peptone.	Leucin, tyrosin, anthrax alkaloid—(?) nitrogenous.
Bacillus diphtheriæ . . .	Ferment	Proto- and deutero-albumoses.	Organic acid.
Epithelial cell of gland (venom gland snake).	...	Hetero-, proto-, deutero - albumoses.	Non - nitrogenous organic acid.

Our conception of the formation of these albumoses in the venom gland of the snake is the following:—The cell, by a vital process, directly exercises hydrating influence on the albumins supplied to it by the blood, the results of which influence are the albumoses which we find in venoms. The difference between this process and the digestion by pepsin or by anthrax bacilli is that in the case of the cells of the venom gland the hydration stops short at the albumose stage, and is not continued so as to form peptone, as is the case with the others mentioned. That the protoplasm of gland epithelium is capable of exercising such hydrating influence is illustrated by the conversion of glycogen into sugar by the liver-cells. It must be borne in mind that, although the albumoses formed by these various agencies have not, so far, been chemically differentiated, yet they are not identical; and when submitted to an infinitely more sensitive test—the physiological test—they produce vastly different results. In view, however, of the essential chemical identity which does, nevertheless, underlie such physiological differences, I may be permitted to express my conviction that the discovery of a method of antagonising the effects of the administration of snake-poison would be a highly important contribution towards the solution of the problem of dealing with the effects of the virulent products in zymotic diseases.

Method of absorption of venom.—Venoms may enter the body by a variety of channels. The onset and train of symptoms vary with the rapidity with which they reach the circulation. In cases of snake-bite the poison is usually deposited in the subcutaneous tissue, whence it reaches the general circulation; principally by absorption through the blood-vessels. When introduced into a serous cavity, absorption is much quicker; and, if introduced directly into a vein, the effects are manifested instantaneously. Venoms are absorbed from the conjunctiva, but, with the exception of cobra venom, do not appear to be capable of exercising any injurious effect when taken by the mouth; provided there be no abrasions of the mucous membrane of the alimentary canal. In this respect they resemble tetanus toxine (Tizzoni).

Venoms exhibit an accumulative action; an animal succumbs more readily to two or three divided doses than if the whole be administered at one time.

Elimination of venoms from the body.—Venoms are excreted by the kidneys and perhaps also by the salivary glands. Richards and Ragotzi found that the urine of an animal poisoned by cobra venom, when injected into a pigeon or frog, produced symptoms of cobra poisoning. During its issue from the body by this channel cobra poison produces no ill effects; but viperine poison, and also, to a less extent, the poison of Australian colubrines, produce a disastrous effect on the structures of the kidney. This subject will be discussed later.

Symptoms of snake-bite in the human subject.—The symptoms vary considerably in different individuals and with different amounts of the same venom. When the effects of the venoms of the two great classes of poisonous snakes are compared, they also exhibit a marked variation. It is necessary, then, to mention the prominent characteristics of ordinary cases of poisoning by different snakes.

Cobra-bite.—The first symptom is a sensation of burning pain, more or less severe, at the seat of inoculation. This spot soon becomes red, tender and swollen. An interval of about half an hour usually occurs before the patient experiences any constitutional symptoms: he then feels intoxicated, sleepy, and weak in the legs; the weakness increases until he is unable to stand. Profuse salivation, paralysis of the tongue and larynx, with inability to speak or swallow, soon supervene. Nausea and vomiting are of frequent occurrence. The paralysis now becomes more general and decided; the patient lies on his back, incapable of movement. His breathing becomes slower and the respiratory excursions diminish; he appears to be conscious, but unable to express himself; the action of the heart is quickened, but of fair strength. At length the breathing ceases, with or without convulsions, and the heart shortly stops. Up to or immediately preceding the respiratory cessation the pupil remains contracted and reacts to light.

the patient may die about twelve hours after the bite. If he recover the depression the local symptoms begin to play a much more tant part than in cobra poisoning. The swelling and discoloration l up the limb and trunk, and symptoms of general blood-poisoning with rise of temperature, puffy face, great weakness, and repeated pe. The pulse is quick and feeble, and the respiration laboured. imes the mind is clear; sometimes there is restlessness and delirium. may occur in this stage, and is sometimes preceded by convulsions. ocal hæmorrhagic extravasation frequently suppurates or becomes enous, and from the results of this the patient may die even weeks ards. When the dose has been a less severe one the swelling may e and pain disappear rapidly. Recovery is in almost every case n and astonishing when contrasted with the gravity of the symptoms; a few hours the patient, from being in a moribund condition, es bright and intelligent.

ite of the European viper.—The symptoms following the bite of the ean viper resemble those of a small dose of rattlesnake venom. ite is immediately followed by local pain of a burning character; nb soon swells and becomes discoloured, and within from one to hours great prostration, accompanied by vomiting and cold clammy ration, sets in. The pulse becomes extremely feeble, and slight œa and restlessness may be seen. In severe cases, which occur in children, the pulse may become imperceptible and the extremities and the patient may pass into coma. In from twelve to twenty- ours these severe constitutional symptoms usually pass off; but in eantime the swelling and discoloration have spread enormously. imb becomes phlegmonous and frequently suppurates. Within a ys recovery usually occurs somewhat suddenly, but death may occur he severe depression, or from the secondary effects of suppuration.

poisoning by the Indian viperine snake the symptoms resemble

Bite of Australian species of snakes.—The pain and local swelling which follow a bite by one of the larger Australian colubrines is not usually severe. Constitutional symptoms appear in from fifteen minutes to two hours. The first symptom is almost invariably a feeling of faintness and an irresistible desire to sleep. On attempting to walk the gait becomes staggering, and the weakness in the legs increases until the patient is unable to stand alone. Alarming symptoms of prostration then supervene, and are often accompanied by vomiting. The heart's action becomes extremely feeble, and the pulse threadlike and uncountable; the extremities are cold and skin blanched. The respiration, which at first is somewhat quickened, becomes shallower from hour to hour as the coma increases. Sensation is blunted, and eventually stimulation of the nerves of special sense ceases to evoke any reaction: the pupil is widely dilated and insensible to light. In this state death may occur from gradual cessation of respiration; it is sometimes preceded by convulsions. The heart, which has become extremely feeble in its action, may sometimes be felt to beat for a few seconds after the cessation of respiration. In some cases hæmorrhagic extravasation also occurs from some mucous surface; so that the patient coughs or vomits blood, or passes it by the rectum or kidneys. Albuminuria has been generally found when looked for, and may be accompanied by blood or blood pigment in the urine. If the patient survive the coma, recovery is complete; and, as a rule, is rapid and without any secondary symptoms.

Morbid anatomy in man.—The number of carefully recorded autopsies is small. In cases of death from *cobra-bite* rigor mortis occurs as usual. The areolar tissue in the region of the bite is infiltrated with pinkish fluid, and the neighbouring vessels are injected. The blood is often fluid, and when examined by the microscope directly after death it presents no changes. The brain appears to be normal; but the veins of the pia mater are usually gorged with blood, and the ventricles often contain turbid fluid. The lungs are usually congested, and the lining membrane of the bronchi is intensely injected. The appearance of the kidneys varies from the normal to one of excessive congestion.

After death from poisoning by one of the *viperine snakes*, the region of the bite is the seat of intense œdema and extravasation of blood. If the poison be introduced into the subcutaneous tissue the underlying muscles are frequently disorganised and even diffluent from extravasation of blood in their midst. Hæmorrhages may also be found in any of the organs and along the alimentary tract. The kidneys are acutely congested or hæmorrhagic. The blood is fluid.

Autopsies in cases of bite by *Australian species of snakes* present, as a rule, the same appearances as those detailed in cobra-bite. The blood is almost invariably fluid, but may contain a few soft coagula. The lungs may be the seat of hæmorrhages; in cases in which blood has escaped from mucous tracts during life these surfaces are intensely congested and hæmorrhagic. The nervous system merely shows congestion of blood-vessels.

Physiological action of snake venoms.—Conclusions as to exact physiological action drawn from the observation of cases of snake-bite in the human subject, while of the greatest importance, are necessarily unsatisfactory, owing to ignorance and want of control of the many factors concerned. When confronted with a case of snake-bite our principal duty is to treat the patient; and, although we may carefully observe clinical symptoms, those more accurate analytical methods which can be performed on the lower animals are impossible. Another disadvantage is that no single observer can witness a sufficiently large number of cases of snake-bite, but must base his conclusions to a great extent upon the observation of others.

On the other hand, it is a long inference no doubt to say that results obtained upon lower animals can be applied to man. Nevertheless, when one considers the identity of mechanism underlying the differences in the higher mammalia, and the fact that such animals react to snake-poisons with striking similarity to man, the inference would not appear to be unjustifiable.

Before considering experimental results obtained upon animals, it is necessary to emphasise the fact that the effects of a venom introduced directly into the circulation may be very different from its effects in cases in which it was introduced by subcutaneous inoculation. These differences, although no doubt dependent upon the varying rapidity with which the poison reaches the blood, are, from the peculiar nature of its action on this fluid, of such a kind as to be misleading. On reference to the portion of this article devoted to the consideration of the action of snake-poisons on blood plasma, it will be seen that the venom of the Australian colubrines (and, as I strongly believe, of all viperine snakes, and perhaps of cobra poison), if introduced with sufficient rapidity into the circulation, occasions extensive intravascular clotting. A venom may reach the blood with a rapidity adequate to cause thrombosis either when directly introduced into the circulation, or when injected in sufficient quantity and in a favourable situation for absorption.

When we see an animal, within a few seconds or minutes after the introduction of the poison, seized with convulsions over which artificial respiration has no influence, and which are closely followed by death, or a state of profound depression, we are naturally disposed to conclude that the poison has exerted its influence merely upon the nervous system. In the case of such symptoms following the introduction of the venom of the species of Australian snakes I have examined, such a conclusion would be erroneous; for by opening the animal just prior to death the venous system will be found to be the seat of more or less extensive thrombosis. Intravascular clotting is also, in my opinion, the explanation of the convulsions which have been observed by various authors rapidly to follow the introduction of viperine venom into animals, which early convulsions form so marked a feature of poisoning by snakes of this kind. Such convulsions must not be confused with the asphyxial convulsions, due to failure of respiration, which immediately precede death from cobra poisoning.

On subcutaneous injection the venom, as a rule, does not reach the blood with sufficient rapidity to cause extensive thrombosis. Under these circumstances the blood loses its coagulability. The opposite conditions are in reality two phases of the same process.

Thus it will be seen that the comparison of results obtained by the two methods of introduction of venom must be made with considerable caution.

Action of venoms on blood and blood-vessels.—When the literature of this part of the subject is examined, we notice the entirely different results obtained by observers experimenting with various kinds of snakes. Cobra poison would appear to exert little effect on the blood; but that it has some action upon it is evidenced by its fluidity in the human subject after death from cobra-bite. Occasionally, too, the mucous discharges from the body are stained with blood. These blood changes are, however, relatively unimportant; and, if an animal survive the nervous symptoms, it passes at once into a condition of complete health.

By the poison of the viperidæ, and to a less extent that of the Australian colubrines, the blood and blood-vessels are considerably affected. The changes affect both the corpuscular elements and the plasma; and also that little known relationship which normally obtains between the blood and its containing vessels.

Effect of venom on blood corpuscles.—When the blood of a mammal is mixed with a solution of viperine poison in a test-tube, the red corpuscles lose their biconcave shape, become spherical and softened, and fuse together into irregular masses. Ultimately the hæmoglobin is dissolved out and the stromata disappear. The hæmoglobin is unaltered, and reacts as regards oxygen in every way as usual. Examination of the bloody fluid found in the local extravasation shows the same dissolution of the red corpuscles with the hæmoglobin in solution.

Action of pseudechis venom on blood corpuscles.—A drop of frog's blood was mixed with an equal bulk of a 0·7 per cent solution of NaCl, containing 1 per cent of venom. The mixture was made on a slide, speedily covered with a cover-glass, and the edges smeared with oil to prevent concentration of the salt solution by evaporation. Within a few moments a disintegration of the red cells occurred. They lost their shape, their nuclei became apparent, and the hæmoglobin dissolved out; afterwards they appeared large and circular, and became more and more indistinct, until finally nothing could be seen of them but shrivelled granular nuclei. These shrivelled nuclei soon began to swell, the granules became less distinguishable, and eventually disappeared. The disappearance of the red cells was so complete that at the end of fifteen minutes there was nothing, except the slight coloration of the field, to distinguish the preparation from one of lymph.

The action on the white cells was much slower. For the first fifteen minutes I could discover no change in them, but they exhibited no amœboid movements. At the end of this time the nuclei in some of them were very distinct, as if fixed by acetic acid. They then became intensely granular, and soon began to swell, and their outlines to grow less distinct, until they disappeared, leaving a small heap of granules to mark their grave.

During this time control specimens under similar circumstances showed no change, and the leucocytes were exhibiting active amœboid movements.

The action of the poison on the corpuscles of pigeons is similar to the bove ; but, with poison of this concentration, the dissolution of the red ells occurs after the lapse of an hour, and proceeds slowly.

The same destruction of corpuscles takes place with the blood of ammals, but requires either a longer time or greater concentration of he venom solution. When the blood of a dog is examined two to three ours after the injection of the animal with the venom, destruction of the ed corpuscles is very marked. On separating the corpuscles by the entrifuge the plasma is seen to be intensely coloured by hæmoglobin in olution ; and if the number of corpuscles, determined by a hæmocyto- eter, be compared with that observed previously to the injection, a iminution, in some cases to one-half the number, is found. When he venom is intravenously introduced there is an extraordinary and mmediate diminution of the white cells. In some cases less than per cent of the original number can be found. In the course of a few ours, if the dose have been a small one and the animal recovers, the ucocytes steadily increase until they may become three or four times s many as before the injection. With subcutaneous injection the rimary disappearance is not marked, but the secondary leucocytosis is lways present. Halford many years ago drew attention to the greatly ncreased number of leucocytes in the blood of animals which succumbed o snake-poison : he also attached importance to some large nucleated ells which he invariably found present on examination eight to twelve ours after death. These cells, however, are not present immediately fter death : they are swollen leucocytes. Further evidence of the de- truction of red blood corpuscles is seen in hæmoglobinuria ; and in the resence of hæmoglobin in solution in the pleura and pericardium, and ven in the aqueous humour. The destruction is especially well seen hen dogs are the animals used.

Besides inhibiting the movements of leucocytes out of the body, this nake venom also interferes with their vital activity in the body, as shown y the following experiment, which is one of a series with similar esults :—

Two small pieces of sterilised sponge, about 1 mm. cube, were septically introduced into the abdominal wall of a guinea-pig. One of hese little sponges had been soaked in 7 per cent solution of NaCl con- aining 1 per cent of venom, the other in the saline solution without the enom. Both sponges were pushed about a centimetre away from the ncision, which was afterwards drawn together by a horse-hair suture and overed with collodion. After two hours œdema occurred around the enom-containing sponge, but not around the other. At the expiration of five hours the animal was killed, and both sponges were carefully withdrawn and plunged into absolute alcohol. Sections of the two sponges treated in the same way presented very different appearances. The control was infiltrated with leucocytes which stained well with ordinary nuclear stains; the other contained leucocytes only near the margins, and many of these were broken down and took the stain badly or not at all. From these sponge experiments I conclude that whereas into the control sponge the leucocytes by their amœboid movements could penetrate unharmed, in the other sponge their activity was paralysed; they succumbed, and were eventually disintegrated by the solution of the venom.

Action on plasma.—One of the most interesting effects of the action of pseudechic venom (and I believe also of the venom of all viperine snakes) is that if a small dose—equivalent to 0·0001 gramme of the dried poison per kilo of body weight—be intravenously introduced into a mammal, it occasions a remarkable increase in the coagulability of the blood, which may culminate in more or less thrombosis. In most cases this is so extensive that the whole arterial and venous system is clotted; but as a rule the coagulation is confined to the portal vein and vena cava, together with more or less clotting in the right heart and pulmonary artery. When extensive solidification occurs it must put an end to life; but when the clotting has been confined to the portal vein, or otherwise limited in extent, and in those cases where only increased coagulability without actual thrombosis has occurred, this phase of increased coagulability is followed in the course of a few minutes by an exactly opposite phase in which the blood clots very slowly or remains permanently fluid. In this state the blood is immune, so far as intravascular coagulation is concerned, against further injections of the venom. When the venom reaches the circulation very slowly the first portions produce this immunity against the remainder of the injection. Poison injected subcutaneously does not, as a rule, cause extensive thrombosis; but if a very large dose be introduced the venom may reach the circulation with a rapidity sufficient to cause intravascular clotting and speedy death. Such a state of affairs occurs when a comparatively small animal—such as a frog, rat, or mouse—is bitten by a large snake; but with larger animals the incoagulable condition of the blood is in the great majority of cases observed alone.

The significance of these phenomena cannot be here discussed; but it may be mentioned that in every respect they exhibit the closest parallelism with the results obtained by Wooldridge after injecting solutions of nucleo-albumins into the veins. In the case of venoms, indeed, no such bodies are introduced; but it is possible that the destructive action of the poison on blood-cells and the endothelial lining of the vessels may determine their presence in the blood-stream.

Examination of the gases in blood after poisoning with venom.—It has been previously mentioned that, beyond setting it free from the corpuscles, snake venoms exert no influence on the hæmoglobin of the blood: it is still capable of taking up oxygen and parting with it as under normal conditions. In an animal poisoned with venom the quantity and also the tension of oxygen in arterial blood, except immediately preceding death when the respiration and circulation are failing, are approximately normal. The absolute quantity and tension of CO_2 are both usually a little higher than previous to the injection. This is easily explained by the diminished respiratory movements and retarded circulation. Artificial respiration reduces the excess to a small extent. As death approaches, both the tension and the quantity of CO_2 contained in the blood increase greatly from the same cause.

Effect on the blood-vessels.—Dr. Mitchell first investigated the mechanism of the phenomena of hæmorrhagic extravasation, which forms so prominent a feature of viperine poisoning. He prepared the mesentery of a warm-blooded animal for microscopical observation on the warm stage, and then applied crotalus venom to it. He noticed an almost immediate dissolution of the continuity of the capillary walls with which the poison came in contact. This occurred suddenly, and was not preceded by any diapedesis of white corpuscles. The blood escaped, without previous indication, from those capillaries which were nearest to an arterial twig, and in which, therefore, the hydrostatic pressure was highest. Ligature of the vessels to the part prevented further hæmorrhage. The same phenomena are observed with the venom of Australian colubrines, but their action is not so energetic as that of viperine poisons.

In the portion of the article devoted to the chemistry of venoms it was pointed out that they all contain in varying amount a proteid coagulable by heat. It is of considerable interest that the viperine poisons which contain such proteids in greatest amount also exercise this destructive action on blood corpuscles and the walls of the blood-vessels; whereas cobra poison, which contains less than 2 per cent of coagulable proteid, only exerts such action to a very slight extent. Boiling, or indeed raising the temperature of the solution to 80°-85° C., entirely deprives venoms of this action; and, in the case of the venoms of Australian colubrines, also of the power of producing intravascular clotting. The venoms are still poisonous after this treatment, but they exercise their toxic effect in an entirely different manner.

Influence of snake venoms on the germicidal action of serum.—Weir Mitchell has frequently drawn attention to the fact that the characteristic local extravasations, as a general rule, suppurate or become gangrenous, and that bodies of animals dead of rattlesnake poisoning putrefy with extreme rapidity. Feoktistow also made the interesting observation that the bloody effusions in the pleura and pericardium sometimes contain micro-organisms immediately after death; and that cultures of these organisms, when injected into healthy animals, produce no effect. Last year Dr. Ewing repeated some of Nuttall and Buchner's observations on the germicidal power of serum, and instituted a series of comparative experiments with the plasma or serum of animals poisoned with crotalus venom. He found that the normal germicidal power of serum was entirely lost after poisoning with crotalus venom. Experiments made in Sydney with the venom of pseudechis have shown that Ewing's results apply also to the blood of animals poisoned by the venom of this snake.

Effect of venoms on circulation; Experiments with the excised heart of frogs.—When the excised heart is fed with a solution of defibrinated blood containing a weak solution of venom, the contractions become slower, smaller, and eventually stop in diastole. If the solution of venom be more concentrated it stops the heart immediately, in partial systole. It is impossible to induce further activity by supplying it with fresh unpoisoned blood.

Action on the heart of mammalia.—By direct observation in the open thorax, Feoktistow observed great diminution in the contractions of the heart after injection of crotalus and other viperine poisons.

Very marked diminution of cardiac activity is characteristic of all kinds of snake poisoning, except perhaps cobra poisoning, in which case the circulatory mechanism is not markedly affected unless the doses be considerable; and the heart is often found beating strongly up to and after death from failure of respiration. The heart-beats are at first increased and then diminished. If the heart be cut off from all centric influence by severance of the cardiac nerves the primary increase does not occur.

Effect on the blood-pressure.—All venoms, whether introduced directly into the circulation in small quantities, or subcutaneously in large doses, produce a sudden and remarkable fall of blood-pressure, during which the animal may die. If it continue to live, the pressure slowly but gradually rises even above the normal. The curve corresponds to that obtained by the injection of large quantities of commercial peptone (albumoses). In the case of pseudechis poisoning the causation of this primary fall, as shown by simultaneous tracings of carotid blood-pressure and the volumes of kidney and spleen, is mainly cardiac. Vascular dilation of the abdominal area, if it occur, is entirely masked by the effect of the cardiac depression. The pressure then remains fairly steady for an interval of half an hour to ten hours, and then gradually declines further. At the same time the animal shows signs of advancing paralysis with dull reflexes, incoördination, pupils dilated and insensitive to light, and respiratory movements of less and less extent. The corneal reflex usually persists until near the end. In the case of cobra poisoning the blood-pressure may remain high almost up to the moment of death, and, during the asphyxial convulsions which terminate life, often rises above the normal.

In experiments in other kinds of snake poisoning the decrease in respiratory *excursus* and the fall of blood-pressure would appear to occur together. Such is the case with poisons from the Australian colubrines; and, although life may sometimes be prolonged for a few minutes by artificial respiration, in no case have I been able to keep an animal alive for hours, as can be done after failure of the respiration in cobra poisoning.

During this second gradual fall of blood-pressure there is evidence of vaso-motor paralysis, as well as of diminished cardiac action. During the temporary recovery from the initial fall of blood-pressure, stimulation of the peripheral ends of the splanchnics produces a small rise in pressure; but after the final fall has once occurred stimulation produces no further effort. The same result occurs with stimulation of the central end of a sensory nerve. Until near the end of life vagus stimulation stops the heart both in cobra and pseudechis poisoning; but Feoktistow came to the conclusion that the vagus-endings in crotalus poisoning were paralysed early.

During the fall of pressure, and especially at first, digitalin, caffein, and ammonia produce a certain amount of rise, provided the animals have not received too large a dose of venom. Transfusion of blood when the pressure is low raises it only so long as the injection is continued.

Action of venoms on the nervous system.—The determination of the exact physiological action of a poison on the nervous system of the higher animals is always difficult. The difficulties are enormously increased when the poison, as is the case with most snake venoms, profoundly affects the blood and the whole circulatory apparatus also. In such a case it is not easy to distinguish effects which are due to the primary action of the poison on nervous tissue, from those which are secondary to changes produced on the circulation and blood.

Wall concludes that the principal action of cobra poison on the nervous system consists in an extinction of function (extending from below upwards) of the various nerve-centres constituting the cerebro-spinal system; and though, no doubt, other parts of the nervous system suffer, cobra poison has a special affinity for the respiratory centre, and those other ganglia allied to it in the medulla oblongata, which are in connection with the vagus, the spinal accessory, and the hypoglossal nerves; it is directly to this destructive action that we have to attribute death in most cases of cobra poisoning.

As previously mentioned, the circulation is well maintained up to or immediately preceding the death of the animal after the injection of cobra poison. If, immediately after the failure of respiration, artificial respiration be resorted to, the circulation may be maintained for a considerable time (thirty hours). Artificial respiration prevents the convulsions which occur on respiratory failure, and which recur on cessation of the artificial inflation.

Brunton and Fayrer, from a series of experiments on frogs and mammals, came to the conclusion that cobra poison, besides paralysing the reflex activity of the cord, acts upon the nerve-endings in muscle as does curare. Ragotzi confirmed Brunton and Fayrer's observations, and is of opinion that paralysis of the nerve-endings in muscle is the chief cause of failure of respiration; also that the direct action of cobra poison on the central nervous system is altogether subsidiary.

The first effect of cobra venom on the respiration is a decided quickening and deepening of the respiratory movement, which, however, is no longer seen after section of vagi. The quickening is but temporary, the respiration soon becomes slower, and the respiratory movement less and less. Eventually the respiratory movement fails to oxygenate the blood, and the animal dies with the usual symptoms of asphyxia.

The poisons of other snakes produce the same gradual paralysis of the reflex activity of the cord, but the respiratory centre is not selectively affected, as appears to be the case with cobra poison: the activity of this centre is more gradually reduced, and finally abolished together with other parts of the nervous system. Accordingly one finds that artificial respiration is unable to prolong life beyond a few minutes at the most. No definite influence on the motor nerve-endings has been detected. When the activity of the nervous system has been paralysed by venoms, the injection of substances such as strychnia and picro-toxin, in doses which usually produce convulsions, cease to have any effect.

On the respiration these venoms exert a double action: first an irritant action on the peripheral terminations of the pneumogastric nerves, by which an increase in respiration is brought about; and, secondly, a depression of the respiratory centres, by which the respiration rate is diminished. Since in animals with cut pneumogastrics the diminution begins directly after injection, and at a time when in normal animals an increase occurs, it is apparent that these two factors are acting at the same time to produce opposite results. Consequently, the increase or decrease in the respirations must be dependent upon the relative degree of power exerted by one or the other of these facts. Ultimately respiration ceases altogether, and usually ceases before the heart-beat. The gradual enfeeblement of the circulation, due to the cardiac weakness and paralysis of the vaso-motor system, contributes to the respiratory failure, and conversely, so that the activities of the two decline together; and the simultaneous paralysis of the rest of the nervous system in most cases prevents any indication of its asphyxial condition.

Effect on temperature.—The effects of venoms on body temperature vary. Sometimes a rise is observed, sometimes a fall. The explanation is that these poisons influence temperature in three ways: (i.) If a dilute solution of venom in a piece of sterilised sponge be aseptically inserted under the skin of an animal, so that absorption is slow, we obtain a maximum of local with a minimum of constitutional effects; and the temperature is invariably raised a few degrees. (ii.) Under the influence of the profound depression which usually follows injection of poison, there is an associated fall in the body temperature. (iii.) In the case of viperine poisoning, together with the intense local œdema and extravasation, the temperature is raised; but it may fall just before death. If suppuration occur the temperature is raised, but in this case the venom is only indirectly concerned.

Further pathological effects.—If the nervous symptoms from cobra poisoning are recovered from, convalescence is wonderfully abrupt; so that, with the exception of the local blood-tinged œdema in the subcutaneous tissue, which does occasionally suppurate, there would appear to be no further pathological effects. The excretion of the poison by the kidneys does not excite pathological changes in these organs, as witnessed by the absence of albuminuria, and the fact that no alteration in kidney structure has been observed.

With the viperine snakes the case is very different. Here, in addition to the great local and wide-spreading hæmorrhage and œdema, which almost invariably leads to suppuration or gangrene, the victim is subject to hæmorrhages in almost all the organs, and from all the mucous membranes of the body; and also to bloody effusions into cavities such as the pleura and pericardium. The lungs are frequently the seat of ecchymoses, infarcts and œdema. The left ventricle of the heart exhibits sub-endocardial hæmorrhages, which may extend to the whole cardiac structure. The kidneys show hæmorrhage into Bowman's capsule, and into the walls of the pelvis; and the epithelium of the convoluted tubes exhibits necrotic degeneration. Albuminuria or hæmaturia is the rule.

The hæmorrhagic effects are not produced to the same extent by the poisons of Australian species of snakes. In this respect, as in many others which have been pointed out, they stand between the venoms of the cobra and the viperidæ. The local symptoms are not severe, but the œdema is always more or less hæmorrhagic. In dogs especially hæmorrhages, similar in situation to those just described, are the rule. The kidneys of these animals exhibit the same extensive necrosis of the epithelium of the convoluted tubes, which I have often seen blocked with crystals of hæmoglobin. In all cases of snake-bite in which I have had an opportunity of examining the urine, it has contained albumin and often traces of blood pigment. In bad cases hæmaturia sometimes occurs. Animals may succumb to the kidney trouble from suppression of urine three or four days after inoculation; but when recovery occurs the albumin or blood disappears from the urine in a few days, even when urine like blood has been passing for twenty-four hours.

Effects on lower animals other than mammals.—Cold-blooded vertebrates require, relatively to birds and mammals, much larger doses to produce death. In them hæmorrhagic extravasations do not form so prominent a feature as in viperine poisoning; they show, however, the same gradual paralysis of heart and nervous system as is seen in warm-blooded creatures. Snakes, especially the venomous kinds, possess a considerable amount of immunity; but they succumb to large doses in the same manner as other reptilia. The action of venoms on such invertebrates as the fresh-water mussel (*Anodonta cygnea*) and the crayfish (*Astacus fluviatilis*) is to produce cessation of the heart-beats.

Snake venoms putrefy as do other albuminous solutions. They do not appear to exert marked influence upon the activities of infusoria or spermatozoa. Cilia from the frog's mouth or the gills of oysters remain active in the venom just as long as in a solution of commercial peptones of the same concentration.

The toxic value of venoms.—Calmette has worked out a table of the relative toxicity of venoms—as Roux and Vaillard have done for tetanus toxines—based on the number of grammes of an animal (rabbit) killed by one gramme of poison subcutaneously introduced. The virulence of less. Eventually the respiratory movement fails to oxygenate the blood and the animal dies with the usual symptoms of asphyxia.

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Cobra	4,000,000
Hoplocephalus curtis (Australian species)	3,450,000
Pseudechis „ „	800,000
Pelias berus	250,000

My own experiments with rabbits place the toxic power of the two Australian venoms higher, namely :—

Hoplocephalus curtis	4,000,000
Pseudechis	2,000,000

Prognosis.—Sir Joseph Fayrer is of opinion that a bite from a vigorous adult cobra—Hamadryad, *Bungaris* or *Daboia*—if the snake has embedded its fangs and inoculated its full charge of venom, is invariably fatal. In many cases of snake-bite the reptile, for a variety of causes, may not succeed in accomplishing this object. In America the mortality in cases of snake-bite is much less. In a series of recorded cases quoted by Weir Mitchell the mortality was 25 per cent, and in Australia it is about 7 per cent. No doubt the mortality in the last two countries would be much higher were not the population well aware of the necessity of the immediate application of a ligature, and of prompt local measures of treatment.

Treatment of cases of snake-bite.—When a person has been bitten by a poisonous snake our efforts to influence the result may take three directions: (i.) To prevent the absorption of the poison; (ii.) To counteract or lessen its effect on the organism; (iii.) To hasten its elimination.

(i.) With the first object one should immediately place a ligature on the limb, above the situation of the bite. The ligature must be tightly applied, and this object is easily attained by passing a stick under the ligature and twisting it. Free incision should then be made into the subcutaneous tissue into which the poison was injected. The wound may be sucked with advantage provided that no abrasions exist on the mouth or lips of the person who performs this office. After free incision an attempt to express the poison should be made by bandaging the limb downwards from the ligature to the region of the bite. An elastic bandage is preferable for this purpose, but would rarely be at hand. This downward bandaging should be repeated several times. Fayrer recommends the application of strong nitric acid, or the actual cautery, to the situation of the bite. A 2 per cent solution of calcium hypochlorite (bleaching-powder), or a 1 per cent solution of permanganate of potash (Condy's fluid), would be equally useful if brought into direct contact with the venom. If the seat of inoculation be a finger or toe, amputation, after ligature, is justifiable in the case of a bite from one of the larger snakes. The time during which the ligature can be kept on is short, as it causes great suffering; after half an hour, if it has been so applied as to obstruct all circulation, it should be removed for a few minutes, and as soon as the circulation has returned to the limb it should be reapplied, and again loosened at intervals. If the ligature has been properly applied so as to obstruct the circulation, it is advisable to discard it altogether after one hour on account of the danger to the limb.

The effect of a ligature applied as directed above is much more efficient than merely to place a temporary mechanical obstacle to the circulation. The anæmia, assisted by the local influence of the poison, profoundly affects the walls of the blood-vessels; this is indicated by the œdema of the limb which follows the removal of the ligature. In this condition absorption is probably much delayed, for rabbits withstand the inoculation of an amount of pseudechis venom equivalent to six and sometimes ten times the fatal dose, with little constitutional disturbance, if an elastic ligature be immediately applied above the seat of injection, and allowed to remain on for twenty minutes.

(ii.) When the venom has once reached the general circulation the chances of combating its effects are not very hopeful. As Dr. Weir Mitchell says, "Unfortunately that which alters the venom as such is always equally destructive to the tissues of the body, and no agent as yet employed can be shown to have the power to enter the blood and there affect the venom without doing harm to other albuminous substances. . . . They can be thrown into the fang-tracks, and where they are made to mingle with the venom will destroy it as impartially as they do the innocent tissues in which it lies."

The remedies which have engaged the most attention of recent years are the intravenous injection of ammonia and the subcutaneous injection of strychnia. Ammonia has been recommended for snake-bite for hundreds of years; but the idea of introducing the remedy directly into the circulation was due to Professor Halford of Melbourne. Until his experiments in this direction, I think no one imagined that such a quantity as a drachm of liquor ammoniæ fortior could be thus introduced at one time with impunity. The remedy was extensively used in Australia in the years 1874 to 1876; and accounts of its success crowded the medical literature of Victoria at that period. In 1876 the Medical Society of Victoria appointed a Commission to inquire into the subject. These gentlemen experimented upon dogs, and came to the conclusion that if the animal received a fatal dose of the venom ammonia was unable to avert death; if the dose were not a fatal one the ammonia did not prevent a favourable termination. Experiments made by the members of the Indian Snake Commission, of which Mr. Vincent Richards was chairman, led the Commission to a conclusion similar to that arrived at by the Victorian Commission. From that time forward the remedy began to fall into disrepute. Professor Halford never imagined that ammonia was anything more than a stimulant, and in his most sanguine moments did not regard it as an antidote in any sense.

The use of strychnia was recommended as a remedy by Dr. Pringle in the *Australian Medical Journal* for September 1868. In 1874, Vincent

Richards experimented with strychnine as a remedy in cobra poisoning. The animals used were dogs, and he found that if the strychnine was pushed they died from the effects of this drug; if it were not, they died from cobra poisoning. Quite recently Dr. Kanthack has made a few experiments with the same result. He concludes: "Nothing, therefore, is to be expected from this treatment, and no false hopes should be raised or fostered as to a cure by strychnia." Feoktistow found that when the animals were under the influence of crotalus venom to such an extent that reflex activity was much diminished or lost, even intravenous injection of strychnine was absolutely without effect. This observer also pointed out that when tetanus has been produced by a previous injection of strychnine snake venom is capable of abolishing the spasms.

In 1889, Dr. Mueller of Victoria very strongly advocated the use of strychnine, which he regarded as an antidote to snake-poison. Since this date hypodermic injection of the drug has been practised on a large scale in Australia; in some cases as much as 1 to 2 grains being introduced. The published accounts of this treatment equal in enthusiasm those of the introduction of ammonia into the circulation. Consciousness and reflex action return in a few minutes, the pulse improves, and the patient is apparently rescued from impending death. At the third Intercolonial Medical Congress in 1892, Dr. Huxtable brought forward some figures which he had collected of the mortality of snake-bite in Australia, and compared the cases in which hypodermic injections of strychnine were administered with those otherwise treated.

	No. of Cases.	Deaths.	Mortality per cent.
Cases treated by strychnine . .	113	15	13·2
Cases treated otherwise . . .	313	13	4·1

These figures show that the mortality of the cases treated by strychnine was more than four times that of other cases. It does not, however, necessarily follow that strychnine is responsible for the increased mortality, for it is in the severer cases that so heroic a remedy could be used. The figures are unsatisfactory in other respects; for in many cases neither the amount of strychnine injected, nor the time which elapsed between the poisoning and the introduction of the remedy, is mentioned. Dr. Mueller particularly insists that the remedy must be administered fearlessly, even until symptoms due to the drug manifest themselves. As in some fatal cases this was not done by the practitioner in charge of the case, the figures for this reason also are not a fair criticism of Dr. Mueller's method.

Considering all things, it appears to me incredible that all these medical practitioners in different parts of the Continent, many of whom had witnessed more than one case of snake-bite, and some of whom were entirely incredulous as regards the action of ammonia or strychnia, could one and all have been mistaken as to the beneficial effect; or that the improvement described can be attributed to coincidence only. Coincidence does, no doubt, explain some cases, for it has been previously pointed out that the medy is equally useful, or to the more logical inference that elief and rapid recovery are peculiarities which belong to those crotalus-bite in which the venom injected has not been so y large as to ensure a fatal ending?" Nevertheless I think we ppose that both these remedies are capable of producing at any porary relief from the cardiac and nervous depression in snake-bite. a and strychnia intravenously injected are both capable of raising l-pressure in animals to some extent, even when it has been reduced lf its original height by a subcutaneous injection of a small quantity n. When the animal is once profoundly under the influence of the however, neither produces any effect.

eviewing the experiments on the lower animals to determine the of both ammonia and strychnia, it has occurred to me that the tests severe, and that too much was expected of the remedies. Cases -bite in man (if we exclude the larger Indian snakes) certainly ecovery as a rule; so that the probability is that the patient does ive much above a minimal fatal dose. In such cases in experi- n animals the treatment has been followed by temporary im- nt (increased inspiration, rise of blood-pressure and contraction of It is therefore possible that in such cases in man, the administra- hese remedies may just tide over the period of depression until on is excreted, and the balance is turned in favour of the patient. he two remedies strychnine has the great advantage of a simple of introduction. Intravenous injections, on the other hand, skilled interference. Ammonia, hypodermically introduced, pro- ost disastrous results, an extensive slough occurring at every point ion.

administration of alcohol has been extensively employed in cases -bite. This has been carried to such an extent that it has often ficult to determine to what extent the symptoms were due to the poisons produced by organisms concerned in zymotic diseases. In recent years no subject has engaged more attention amongst bacteriologists and the medical profession than that of artificially immunising animals against the action of these poisons, and the fact that the serum of such immunised animals possesses antitoxic properties.

Sewall first by repeated injection of small doses of venom produced resistance to rattlesnake poison. He had to proceed very warily, but in five months his pigeons would withstand seven times the fatal dose for control animals. Dr. Kanthack succeeded in obtaining some resistance to cobra poison, but was unable to obtain any real immunity. More recently Phisalix and Bertrand induced some resistance in rabbits by repeated injections of the venom of the European viper which had been previously heated to 80° C.; and M. Calmette, working in Professor Roux's laboratory at the Pasteur Institute, has made a series of experiments with the venoms of a variety of snakes (including the cobra, European viper, and some Australian species) analogous to those made by Tizzoni and Cattani, Behring, Kitasato, and Roux and Vaillard, with tetanus and diphtheria toxines. Calmette employed Roux and Vaillard's method of attenuating the venom by the previous addition of calcium hypochlorite, and then repeatedly injected the solution at intervals of one or two weeks. By any of such methods a certain degree of resistance is produced.

Dr. Kanthack was the first to examine the serum of such partially immunised animals for antitoxic properties; but he came to a negative conclusion. The results recorded by Calmette and Phisalix and Bertrand are more encouraging. The former observer found that 5 c.c. of serum from a fairly immunised rabbit, if administered within one hour, was capable of curing another rabbit which had received twice the fatal dose of cobra poison. After one hour and up to one and a half hours two-thirds of the animals recovered; and if a longer interval were allowed to elapse the serum greatly lengthened the interval before death.

Calmette has also recorded some equally beneficial results from the subcutaneous injection of calcium hypochlorite. I have repeated his experiments under what I imagine to be precisely similar conditions, using the same animals—rabbits; but my results, which are consistent, are entirely negative. It cannot be that I did not inject a sufficient amount of hypochlorite solution, for I first ascertained the maximum dose of my solution which I could introduce with impunity. Having ascertained the minimum fatal dose per kilogramme of rabbit, my animals died with absolute regularity according to whether they were a little under or a little over the standard weight; and this occurred whether they were injected with the solution of the hypochlorite or not. I am quite unable to explain this discrepancy of results, for some of the venoms used by M. Calmette were of the two species of Australian snakes employed by myself.

Calmette found the immunising power of his serum was destroyed by heating to 60° C.

That the key to the treatment of snake poisoning is along the lines of serum therapeutics would appear probable. Behring has shown the value of antitoxic serum in poisoning by diphtheria toxines and cultures. Ehrlich has found that the serum of animals rendered immune to the toxic proteids of jequirity and castor oil seeds is also possessed of antitoxic properties. The analogy between venom proteids and the toxic agents in these plants and in some zymotic diseases has already been pointed out.

Finally, in June 1895, Professor T. R. Fraser communicated the results of experiments which he had been conducting for some time past on the immunising of animals against the venom of the cobra and other serpents, and on the antidotal properties of the blood serum of immunised animals. These experiments absolutely confirm the work which Calmette had published in the previous year.

Fraser from his immunised rabbits has obtained serum possessed of very considerable antitoxic powers. His experiments with the protective serum are divided into four series. In the first series, a certainly lethal dose of venom—capable of causing death in five or six hours—was mixed with the serum and injected under the skin. So small a quantity of antitoxic serum as ·004 c.c. per kilogramme of the weight of the animal was, under these circumstances, sufficient to prevent death. When the dose of venom was doubled, ·6 c.c. was requisite; and 2 c.c. of serum per kilogramme counteracted the effect of four times a fatal dose.

The fourth series gives the clearest indications of the antidotal value of the serum. In these experiments the serum was injected half an hour after the introduction of the poison. When twice a fatal dose had been given, 5 c.c. of the serum per kilogramme of the weight of the animal was sufficient to prevent death.

The experiments of Phisalix and Bertrand, Calmette, and Fraser have established, then, on substantial evidence, that the blood serum of animals protected against large doses of venom is able to prevent death in non-protected animals by lethal doses of venom of the most poisonous snakes; and the treatment, so far as one or two cases go, seems to be equally efficacious in man. From the records of cases of snake-bite, it would appear probable that even in India the victim in the majority of cases does not receive much over a minimum lethal dose. It must be borne in mind, however, that the amount of serum which it is necessary to inject increases proportionately with the weight of the animal. In one of Professor Fraser's experiments, which has been quoted above, the injection of 5 c.c. per kilogramme of the animal's weight, half an hour after the introduction of twice a minimum lethal dose of venom, was followed by recovery. Assuming the conditions to be the same in the case of a man of eleven stone, it will be necessary to introduce 350 c.c. of serum to produce the same result. Such a quantity would be unwieldy to inject; and the expense involved in immunising an animal of sufficient size to produce such an amount of serum would be so great as to exclude the remedy from practical application. There is, however, no reason to suppose that the limit of the antitoxic power of the serum of artificially immunised animals has as yet been reached, or nearly reached. If the present methods be still employed, further and further quantities of venom must be introduced into the immunised animal. In this way the bulk of the doses of the serum will be reduced as the antitoxic value of it is increased; at the same time, however, its production must become more and more expensive. [See later, pp. 836, 837.—Ed.]

The next important advance in the pathology of the zymotic diseases may be the discovery of the principle which underlies the action of curative serum. Calmette has demonstrated that the antitoxic value of the serum of animals immunised against snake-poison is not due to a direct action of the so-called antitoxine on the poison; and this conclusion is probably equally true with regard to the antitoxines against diphtheria and tetanus. If, then, it does not operate upon the toxines directly, it must exert its beneficial effect indirectly, by influencing the activities of the tissues of the animal. The question which demands an answer is: How does antitoxine serum place the cells of the animals in a position to resist the poison? When the venom of the Australian black snake is subcutaneously injected into a dog it produces, amongst other results, an extensive disintegration of the red blood corpuscles; but I have found that, if the animal be previously injected with the serum from another dog which has been immunised against this venom, this destruction of red corpuscles does not occur; or, if so, to a trifling extent only. In such a case as this, did the antitoxic serum induce a change in the red blood corpuscles, or had it so stimulated other cells in the body that they destroyed the toxine, which therefore never came to operate upon these corpuscles? The study of the manner in which antitoxines affect the *details* of the toxicological action of all these poisons will no doubt afford a fruitful line of research. There is no toxine of which the details of the physiological action are so well known as those of some varieties of snake-poison. This poison is therefore well adapted for such an investigation. Snake-poison also possesses the great advantage over most other toxic proteids that it is much less sensitive to the operation of physical agencies, such as light and heat, and is comparatively easy to obtain in a form which preserves a remarkably constant composition.

The efficacy of this treatment of snake poisoning in animals seems then undoubted; but it is not yet in a position to put off the swaddling-clothes of the laboratory, and to take its place in our system of practical therapeutics. The antitoxic power of the serum must be enhanced, or a method discovered by which the active agent or agents may be separated from the serum. There will probably be no great difficulty in attaining the former end; and the separation of the hypothetical "antitoxine" will no doubt be accomplished at no very distant date. When this is done, the only difficulty in supplying the antitoxine in quantity will be a commercial one. To prepare such a supply large animals must be immunised. This, however, at the present time, necessitates the employment of a considerable amount of snake venom, and this venom is a costly commodity.

(iii.) Concerning the value of the third method, by hastening excretion, there are no accurate records. The poison has been shown to be excreted by the kidney; but whether diuretics exercise any effect in averting a fatal issue has not been determined.

From the above considerations it would appear that whatever leaning the individual practitioner may have towards this or that mode of constitutional treatment, every endeavour must be made to prevent absorption of the poison. Some form of ligature can be extemporised, and we have undoubted evidence of the worth of this treatment; whilst the value of every attempt to combat the effects of the poison after it has entered the blood is yet undetermined. The danger is lest our anxiety to find some real antidote to snake-poisons may in the meantime divert our attention from the ligature and local measures; and that in immature attempts at antidotal therapeutics we may lose sight of a very real and important means of averting death.

CHARLES J. MARTIN.

APPENDIX BY DR. CALMETTE

Treatment of snake-bite by the anti-venomous serum.—Since the completion of the preceding article by Dr. Charles Martin, our knowledge of the several venoms, and of the treatment of their inoculation, has made some advances which must be reported here.

This new knowledge is chiefly the result of the work on the subject which I have continually carried on for some years past, and which has been ably and fully confirmed by Professor Fraser of Edinburgh.

I have had the opportunity of studying the venom of the following reptiles:—Naja tripudians, Crotalus durissus, Bothrops lanceolatus, Naja haje, Cerastes ægyptiacus, Bungarus fasciatus, Pseudechis porphyriacus, Hoplocephalus curtis, H. variegatus, Acanthophis antarcticus, Trimeresurus viridis, and Trigonocephalus contortrix.

The venoms of all these snakes respectively have well-marked toxic peculiarities, and produce their several and various local phenomena. Nevertheless, I have ascertained that animals rendered immune by vaccination against a dose—say of Cobra or Bothrops venom—many hundred times the ordinary fatal dose, resist likewise inoculations of very powerful doses of the venom of any one of the other serpents I have enumerated.

The proportion of dry residue obtainable by evaporation, at the ordinary temperature of the room, of the venom discharged by a serpent at each bite is very variable, and depends amongst other conditions upon the longer or shorter fast to which the animal has been submitted. Generally speaking, this proportion fluctuates between 25 and 35 per cent; thus the larger venomous snakes, such as the Naja tripudians or the Bothrops, scarcely give, on an average, more than fifty milligrammes of dry residue at each bite.

By very careful management the larger animals, such as the dog, the ass, or the horse, can be habituated to larger and larger doses of venom. Thus we are enabled to inject a hundredfold and more of the ordinary fatal dose without setting up any symptoms of illness. The intervals between the injections must be sufficient to allow the animal to recover, and to regain its normal weight. After some time, say in twelve or fifteen months, the serum of the protected animal has acquired a preventive capacity of such a standard that if a rabbit be injected with $\frac{1}{200000}$ of its own weight with this serum it will not succumb to a dose of venom, inserted twelve hours later, which proves fatal to a control rabbit of the same weight.

At the Pasteur Institute at Lille, where large quantities of the antivenom are prepared, we make use of horses; several of these horses have been made immune for two years. Quite lately control experiments with the Lille serum were made at the Conjoint Laboratories in London before a committee of scientific men. These experiments showed that the therapeutic power of the serum is now such that if a series of animals —of rabbits, for instance—be inoculated with a uniform dose of a venom which, in this dose, would kill in two hours, and if in one hour and a half 5 c.c. of the serum (assuming the rabbit to weigh two kilogrammes) be injected into a vein, a fatal result will be prevented.

The antivenom has been tried on man in a few cases in India, in Indo-China, in Martinique, and on the West Coast of Africa—cases in which the species of the biting serpent could be definitely ascertained. In these cases the doses of serum injected into the victims varied from 10 c.c. to 20 c.c.—doses which sufficed to dissipate all the symptoms of serious intoxication, which had already presented themselves.

The best place for the injection of this serum, as of the antidiphtheritic serum, is into the cellular tissue under the skin of the belly.

The antivenom is distributed in doses of 10 c.c. in a liquid form. It will keep active and sound for at least a year. Doses of venom a year old, which, moreover, had been taken to India in the hot season, have been tested, and their potency was found almost intact.

To test this I proposed to the London committee a very simple process, which could be applied by any medical man. The method is this: the dose of a given venom which will kill a rabbit in 20 minutes is ascertained; then into the veins of the ear of two rabbits of about the same weight are injected 2 c.c. of the serum to be tested. A quarter of an hour later a dose of venom sufficient to kill in twenty minutes is injected into the vein of the other ear in each, and into two control rabbits; the controls die, but the two first rabbits should resist the poison. If so, the serum thus proved is fit for therapeutical uses in man, and has a preventive value of $\frac{1}{200000}$. This test can be carried out in half an hour, and the results are definite.

But the employment of the antivenom in the general treatment of intoxication by snake-bite must not lead to neglect of any of those precautions which tend to prevent the absorption of the venom—such, for example, as the ligature of the bitten limb at its origin, and irrigation of the wound with a solution of fresh hypochlorite of lime (1 in 60), or of chloride of gold (1 in 100).

My experiments have shown that the hypochlorite of lime completely destroys the venom deposited in the wound; and that it is more rapidly diffused in the veins than the other substances hitherto recommended as antidotes. If Dr. Martin has failed to get good results in his trials on rabbits, I think he must have used more concentrated solutions, which are less active and produce eschars; or he may have used solutions poor in free chlorine. The solution must be freshly made, kept in coloured phials out of the light, and diluted for use to one-sixtieth; thus the value in chlorine stands about 800 c.c. of chlorine per 1000 c.c. of the solution.

If good hypochlorite of lime is not to be had it is better to use the solution of 1 in 100 of chloride of gold, which destroys the venom, whether in a test-tube or in a wound, equally well; but it very quickly combines with the anatomical elements of the tissues.

The quantity of dry venom, expressed in terms of cobra poison of ordinary activity, required to kill a horse is 15 milligrammes. Five milligrammes will kill a big dog in six or eight hours. Hence we infer that the fatal dose for a man is somewhere about 10 milligrammes. In the dog the dose of antivenom needed to avert death, an hour after the inoculation of 6 milligrammes of dry venom, is 10 c.c.: we may assume, then, that this dose would generally suffice to stop the intoxication in man—even, indeed, if the dose of venom were slightly larger; as man is more resistant to the poison. In all cases a second injection of 10 c.c. should be made some hours after the bite in order to hasten the elimination of the venom, and to reinforce the resistance of the cells of the organism against the toxine.

The immunity against the venom conferred by the antidotal serum is very transient, lasting only from twenty-four hours to ten days, according to the dose injected. I have shown that it depends upon an "insensibilisation" of the cells in respect of the venom; but the venom is not destroyed—not even if it be mixed with the antivenom in a test-tube.

If we mix a lethal dose of venom with a corresponding dose of the serum in a test-tube we shall find that this mixture, if injected into an animal, has no injurious effect. But let us heat the mixture to 70° C. for ten minutes, and then inject it into another animal; we shall now see the latter dies as if it had received no antidote at all. From this we conclude, first, that to heat the antitoxic serum to 70° C. is to destroy its antitoxic quality; secondly, that in the mixture of serum and venom the venom remained intact by the side of the antitoxic serum. When, therefore, we inject the two substances simultaneously the serum must interfere with the action of the venom by means of an almost instantaneous reduction of the sensibility of the cells; the venom being slower in its effects. We cannot, then, regard the serum, whether in the test-tube or the animal, as the vehicle of a substance which is chemically antidotal in the sense of destruction or modification of the venom.

These facts, and the decisive experiments which I have cited, show that the antivenom constitutes a truly scientific method, based upon experiment, of preventing poisoning by the bite of venomous serpents; and that the application of the method to man and to domestic animals bitten by serpents should be extended as rapidly as possible in the countries concerned. This is not merely a matter of common humanity, but one also of public economy; for in India alone, according to official statistics, more than 22,000 persons, and more than 60,000 head of cattle, die annually of snake-bite.

The various Governments and great companies ought to establish posts of medical aid, in ambulance fashion, at least in the chief centres of agriculture and forestry; at such posts all persons bitten could be attended to in the shortest time possible. At every post a supply of serum would be provided, as well as a continually fresh solution of hypochlorite of lime, and other useful medicines and appliances.

The expense of such a provision would be trifling when compared with its great services. The only difficulty, as Dr. Charles Martin has said, would lie in the supply of the large quantities of venom necessary for the immunisation of the horses from which the antidotal serum should be drawn. For this reason we beg, in conclusion, all physicians, and all other persons interested in this matter, to be good enough to help us in our work, by sending to us—at the Institut Pasteur, Lille, Nord-France—the largest possible quantity of dried venom; and also their observations in cases of snake-bite treated with the serum.

A. CALMETTE.

In a second article on the "Natural Immunity of Venomous Snakes" in *Nature* (10th Dec. 1896), Dr. Kanthack gives an account of further researches by Dr. Cunningham (*Scientific Memoirs by Medical Officers of the Army of India*, 1895, ix. pp. 1-30). Most snake-poisons belong to one physiological group, and yield to the same antidote; but Dr. Calmette's serum, prepared against cobra venom, has no effect against daboia venom. This Dr. Kanthack had anticipated from the different nature of these two poisons. Thus Behring's law that distinct toxines require distinct antitoxines is still valid. Dr. Kanthack goes on to prove, from work of his own and of Dr. Cunningham, that the immunity of snakes in general to all or most of these toxines is not due to the presence of antitoxines in their serum; nor is the serum of a cobra or daboia protective against the bites of these animals respectively. Innocent snakes, indeed, are likewise resistant. It is not generally true, as we know, that the serum of animals naturally immune has any protective influence in susceptible varieties. In cold-blooded animals Cunningham thinks that the low respiratory value is a factor of great importance in immunity to cobra venom, though this immunity does not wholly depend upon it.—ED.

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C. J. M.

ALCOHOLISM

In this article reference is first made to the physiological action of alcohol. A few remarks are then made on the various common alcoholic drinks. The phenomena of drunkenness and of acute alcoholic poisoning are briefly described. The causes and the whole subject of chronic alcoholism are next dealt with; and, lastly, an account is given of delirium tremens.

Ethylic alcohol (C_2H_5HO) is the member of the alcoholic series found in wines and good spirits. When alcohol is obtained directly from sugar ethyl alcohol is formed alone, but when indirectly, by transformation of starch into sugar, some amylic alcohol (Fousel oil) ($C_5H_{11}HO$) always appears with it.

Absolute alcohol always contains 1-2 per cent of water, has a specific gravity 0·793 at 60° F., and boils at 78° C. (173° F.)

Rectified spirit contains 16 per cent of water; proof spirit contains 49·24 per cent by weight of alcohol and 50·76 of water, and it has a specific gravity of 0·92. (Spirit above "proof" when ignited fires gunpowder; spirit under proof does not.) Every additional 0·5 per cent of absolute alcohol above 0·92 is said to be one degree above proof (22).

The following *tests* among others may be employed for the detection of alcohol:—

(i.) The production of acetic ether. To the aqueous solution suspected to contain alcohol acetate of sodium and sulphuric acid are added, and heat is applied. If alcohol be present a smell of acetic ether is evolved.

(ii.) The production of iodoform. The suspected liquid is heated in a test-tube with iodine and caustic potash; yellow crystals of iodoform are formed if alcohol be present. This is a delicate test, and will detect alcohol even in the proportion of 1 in 10,000.

(iii.) The reduction of chromic acid to oxide of chromium. A crystal of chromic acid is heated in the solution supposed to contain alcohol; a green colour is developed if it be present. This is a good test in the absence of other reducing agents such as formic acid.

Physiological action.—*Digestive System.*—In the mouth alcohol gives rise to a feeling of warmth and, reflexly, to a flow of saliva. In a similar manner it is thought that it may dilate the vessels of the brain, thereby stimulating it (Brunton). *In the stomach* the vessels become dilated, and the secretion of gastric juice is increased. Large quantities of strong alcohol act as an irritant poison on the walls of the stomach, inhibit the gastric secretion, and in extreme cases produce shock which may be fatal. If the initial shock pass off absorption takes place, and the poisonous effects of alcohol on the various tissues and organs of the body then become manifest. The presence of alcohol or of alcoholic liquors hinders artificial digestion.

Circulatory system.—Alcohol forms a compound with the hæmoglobin of the red blood corpuscles, which takes up and parts with oxygen less readily than normal hæmoglobin; this leads to a general diminution in the metabolism of the body, and as a result the amount of fat in the body may become increased. After the administration of alcohol the heart beats more forcibly and with greater frequency, the period of diastole being shortened; the peripheral vessels are dilated, and thus the familiar flushing of the skin is produced. The pulse becomes full and frequent, the circulation more rapid, and the blood passes into the veins in a less venous condition and containing more oxygen than usual. The increased force and rate at which the heart contracts are due to the reserve power of the organ being called upon, and only last for a time.

As these effects pass off the heart beats less powerfully and more slowly; so that the sum of the two phases is much the same as if no alcohol had been taken. Large quantities, however, diminish both the force and frequency of the heart from the first.

Central nervous system.—Alcohol has first of all an indirect effect; by its action on the circulation it supplies the brain and spinal cord with more blood and so increases their activity: it acts, however, directly on the nerve-cells as a functional poison. Hence though first stimulated by alcohol the central nervous system becomes subsequently depressed. The higher centres connected with mental activity suffer first; after the cerebrum the cerebellum and cord are affected, and last of all the automatic centres in the medulla controlling the vaso-motor, respiratory, and cardiac movements become paralysed.

Metabolism.—Partly as a result of its action as a functional poison on the tissues of the body, and partly from its influence on hæmoglobin, the metabolism of the tissues is diminished by alcohol. It is generally held that the urea, sulphates, and phosphates in the urine are diminished under the influence of alcohol; Parkes, however, found that dietetic doses of alcohol did not alter the excretion of nitrogen, and concluded that in a healthy man on a uniformly good diet alcohol does not interfere with the metabolism of nitrogenous tissues. Chittenden found by experiment that alcohol increased the excretion of uric acid 100 per cent; the elimination of urea and total nitrogen were, however, diminished. The output of carbonic acid gas by the lungs is diminished. The increase in fat which follows the constant use of some alcoholic drinks, such as beer and porter, is due partly to the sugar contained in them, and partly to general alteration in metabolism: it cannot be explained on the supposition, sometimes put forward, that the alcohol is burnt off at once and supplies the energy which is normally obtained from the catabolism of the tissues; and that, as a result of this "protective oxidation," the fat accumulates in the body. Small quantities increase the output of work done for a time, but as the stimulating effect passes away the capacity for work falls considerably; its action thus consists in bringing out the reserve powers for a short effort, and not in restoring or husbanding sources of energy. The experience gained from long marches of troops is that the use of alcohol tends to diminish the total amount of work done. It may enable a man "to spurt," but not "to stay." It is dissipative rather than conservative of energy.

Temperature.—As a result of the dilatation of the peripheral vessels, and the large amount of blood passing through the cutaneous areas, the loss of heat by radiation and convection is greatly increased. About this there is no question. With regard to the influence exerted on the production of heat most of the evidence goes to show that metabolism is diminished, and thermogenesis less than normal.

Experiments on rabbits, however, by Bevan Lewis and by H. C. Wood and Reichert point to some increase in the production of heat at the time when the loss of heat is at its maximum. The mechanism of this thermogenesis is obscure. In a number of experiments on a healthy man, Parkes found that when small quantities of alcohol were taken the temperature was very slightly affected. In some exceptional cases it would appear that alcohol raises the temperature; thus high fever occurs in some cases of acute alcoholic poisoning, where no other cause for the raised temperature is forthcoming.

The outcome of our experience and knowledge is, nevertheless, that alcohol tends to lower the temperature by increased loss of heat, and, to some extent, by lessened oxidation; while the power of the body to resist cold is much reduced by it. This antipyretic action is slight when compared with that of such drugs as kairin, quinine, or antipyrin, and in order to produce any therapeutic effect in fevers toxic doses would be required. In men, and in lower animals accustomed to alcohol, the temperature is little if at all depressed by its administration.

Physiological amount.—Taken in small quantities alcohol acts as a stimulant to the bodily functions generally, and especially to the vascular and nervous systems; large doses have a directly depressing or narcotic effect. The amount of alcohol which can be taken daily for long periods without producing any pathological results varies, of course, with the age, surrounding conditions, and idiosyncrasies of the individual; but for an average person what may be called the physiological amount is about one ounce of absolute alcohol. Parkes and Wollowicz found that one and a half ounce was the physiological amount. But, as Dr. Sidney Martin points out, although this result was true for "two strong healthy men accustomed to alcohol in moderation," it is safer to take a lower standard for the average town inhabitant.

In physiological quantities alcohol may be considered *as a food*, inasmuch as it is used up in the system and is productive of energy; but there is no doubt that healthy and young people are better without alcohol. As age advances it becomes useful, and is of course of very great value in such morbid states as fevers, collapse, etc.

Elimination of alcohol.—Moderate amounts of alcohol are assimilated by the tissues and used up in much the same way as carbohydrate foods, and leave the body as carbonic acid gas and water. Some may pass off as alcohol by the lungs. The fæces do not contain any of the alcohol taken by the mouth. Dr. Bodlaender (quoted by Binz) (26) found that in healthy persons, at most 3 per cent of moderate quantities of alcohol could be recovered from the body. When excessive doses have been taken it may appear in the urine, just as sugar may under similar conditions. This fact does not prove that alcohol when taken in proper quantities is not a food.

Alcoholic liquors.—The physiological effect of alcoholic drinks is partly due to the ethylic alcohol they contain, and partly to the presence of additional bodies. Sugar and dextrin may be useful as foods, while the ethers and salts may be of use in furthering the processes of digestion; and, again, other members of the alcoholic series—amylic, butylic, and propylic alcohol—furfurol and definite adulterations, when present, may exert a decidedly toxic action; so that a dose of such a fluid may be more deleterious than the same amount of alcohol. The physiological effect of alcoholic drinks does not therefore correspond exactly with those of alcohol.

Alcoholic liquors may be considered as:—

(i.) Beer, porter, cider, etc.; (ii.) wines; (iii.) spirits; (iv.) liqueurs, and (v.) other alcoholic solutions taken purely to produce intoxication, such as ether.

(i.) *Beer, Porter, Cider, etc.*—English beer contains about 5 per cent by weight of alcohol, besides extractives, salts, sugar, dextrin, lactic acid, and lupulin, the active principle of hops. Lupulin exerts a depressing action on the nervous system, producing sleep. Lager beer contains less alcohol and rather less sugar; stout and porter are richer than beer in the amount of sugar they contain.

Sweet cider contains sugar, and readily undergoes fermentation, becoming changed into rough or hard cider. There is danger that during fermentation the process may go on to the production of acetic acid and render it sour. Sour cider may set up colic, diarrhœa, and intestinal disturbances. Cider contains malic acid. If cider be allowed to act on lead some of the metal is dissolved: lead poisoning was shown to be due to this cause by Sir George Baker in 1767. Cider contains from 5 to 10 per cent by measure of alcohol.

Perry, like cider, is allied to wine rather than to beer; it contains about 7 per cent by measure of alcohol.

Beer, porter and stout lead to an increased storage of fat in the body. When cirrhosis of the liver results, it is very often found to be associated with much fatty change in the organ. These liquors may give rise to dyspepsia, but not in nearly so marked a degree as the more concentrated spirits; and they are undoubtedly a prolific source of gout. Partially fermented or sweet cider tends to gout, which is not the case with fully fermented or rough cider.

Beer has been adulterated in many ways. Picric acid, strychnia, quassia, and chiretta have been used instead of the hop bitters. Cocculus indicus, which contains the neutral principle picro-toxin, is probably added for the same reason. Opium, for its narcotic effects, and salt, presumably to increase thirst, have been added.

(ii.) *Wines* are obtained from the fermented juice of the grape. When all the glucose becomes changed into alcohol the wine is called "dry"; if some sugar remain the wine is called sweet. The "body" of a wine depends on the amount and blending of the solids (sugar and extractives). By the term "bouquet" is meant the perfume to the nose; and by "aroma" the effect on the posterior nares when the wine is on the back of the tongue. The bouquet and aroma are both due to the compound ethers, especially to œnanthic ether. The maturing of wine is the process of development of these ethers. Roughness is due to tannic acid.

Natural wines contain 5 to 14 per cent of alcohol; 14 per cent of alcohol in a solution stops the fermentation of sugar, so if a higher percentage of alcohol be found, it is due to the subsequent addition of alcohol. Wines, such as Port, Sherry, and Madeira, to which spirit has been added, are said to be fortified or brandied.

White wines are made from white grapes, or from red grapes the skins of which have not been left in the fermenting juice or "must"; in the case of red wines the skins of purple grapes remain in the must.

Sparkling wines have this quality in virtue of carbonic acid, formed during fermentation, which is retained in them; as in Champagne and sparkling Hock. Some sugar is usually added to Champagne before it is finally bottled for the market.

The colouring matter of wines is precipitated in the crust; hence wines become lighter in colour on keeping.

Constituents of wines.—After alcohol the most important factors in wine are the acids, the amount of sugar, and the ethers.

There is no tannic acid in the juice of the grape; it is obtained from the skins and the pips. Malic and tartaric acids are found in the juice. The acids act on the alcohol, and thus lead to the development of ethers; but in good wine the amount of acid should not exceed 5 per cent. Clarets, Bordeaux, and Hungarian wines contain tannic acid; Hocks, Moselle, and Chablis are acid from the presence of tartaric acid, and do not contain any tannic acid. Acid wines on keeping deposit a crust of acid tartrate of potassium, tannin and colouring matters which is at first copious; but subsequently it becomes scanty, and then, when floating in the wine, is known as "beeswing."

Sugar.—In natural wines all the sugar may be transformed into alcohol; in fortified wines the added spirits check fermentation, so that the sugar remains unchanged. Sweet or liqueur wines, such as Tokay, Malaga, Constantia and Tent, contain a large amount (20 per cent) of sugar. Sometimes, on keeping, these wines become ropy from the sugar fermenting into a form of mucilage.

The flavour of wine is due to (1) œnanthic ether and (2) a series of bodies called ethers, constituting the "blume."

Wine contains, in addition to acid tartrate of potassium, tartrates of sodium and calcium.

The following classification given by Sir A. Garrod is a convenient one:—

(*a*) Spirituous wines, containing a considerable quantity of saccharine or unfermented matter, and an amount of alcohol, usually above 15 per cent by weight. The chief wines in this class are Port, Sherry, Madeira, Marsala.

(*b*) Liqueur wines, containing much sugar—Tokay, Malaga, Tent, Constantia, etc., the higher Sauternes; percentage of alcohol between that of the 1st and 3rd classes.

(*c*) Acidulous wines, rich in acid tartrate of potash; alcohol not much above 10 per cent. (*a*) With tannin and colouring matters—

Clarets or red Bordeaux wines; red Burgundies and Hungarian wines; (β) Without tannin or colouring matters—Hocks, Moselle, Chablis, and the light dry Sauternes.

(*d*) Effervescing wines, containing unfermented matter and free carbonic acid—Champagne, sparkling Hock, and Moselle, and sparkling Burgundy.

	Alcohol.	Sugar.	Acidity.
Claret	8-13	. .	·6
Burgundy . . .	11	...	·6
Moselle	12	...	·6
Hock	7-14	..	·6
Champagne . . .	6-13	8-17	·58
Port	15-23	6	·5
Sherry	15-25	2	·4
Madeira . . .	17-22	3	·48
Marsala	16	3-5	·6

(iii.) *Spirits.*—Whisky, gin, rum, and brandy contain alcohol in considerable amount, water and the compound ethers to which their characteristics are due. There is a little sugar in gin, but none in the others. Spirits, from the large amount of alcohol in them, produce more marked dyspepsia than beer, but have much less tendency to set up gout.

While the concentration of the alcoholic drink is the important factor in the development of symptoms connected with the alimentary canal, the total amount of alcohol—whether it be taken as wine, beer, or spirits—is the important factor in determining nervous symptoms.

Whisky (sp. gravity ·915) contains from 50 to 60 per cent of alcohol. It is obtained from malted grain, usually barley, and contains some amylic alcohol, which tends, however, to disappear in the process of mellowing. For this reason whisky should always be kept for at least two years, and for ten if possible; if taken when newly made it produces furious intoxication.

Amylic alcohol has an acrid taste, and gives a peculiar smell to the breath. Ethylic alcohol does not affect the breath. The vapour of amylic alcohol irritates the respiratory organs, giving rise to cough and a feeling of suffocation, and produces headache. The general intoxicant effects of ethylic and amylic alcohol are much alike, but whisky may also contain furfurol, which has a convulsive action.

Originally almost colourless, whisky gets its colour from the sherry or other casks in which it is stored. It may be adulterated with methyl alcohol, creasote, etc.; and, besides causing gastritis, it has usually been credited with a special aptitude to produce cirrhosis of the liver.

Gin (Geneva), or Hollands, is obtained by distilling unmalted grain. It contains a somewhat varying amount of alcohol (49-60 per cent), and a little sugar. It is flavoured with oil of juniper, to which its diuretic action is due. Gin may be considered as a flavoured and rectified variety of whisky; it has much the same effect as whisky. It has been adulterated with sulphuric acid, sulphate of zinc, alum, cayenne, and paradise seeds, the importance of which has been somewhat exaggerated (W. Blyth).

When sweetened and diluted by the retailers gin is known as gin cordial or "Old Tom."

Unlike whisky, brandy and rum, it does not improve by keeping.

Rum is obtained from molasses; it is flavoured by butylic ether, and has an alcoholic strength of 50 to 70 per cent.

Brandy varies in alcoholic strength from 35 to 45 per cent. Cognac and the better kinds of brandy are distilled from wine; ordinary brandy is, however, often obtained from malt. The flavour is due to œnanthic ether derived from the wine from which it is distilled.

Brandy is supposed to be particularly apt to give rise to delirium tremens.

Arrack is the fermented juice of the cocoa-nut tree, palmyra, and other palms; common kinds are obtained from rice. The alcoholic strength is 52 per cent. Hindoos and Malays consume much of it. Indian hemp is sometimes put in to poison the drinker.

Koumiss is obtained from fermented mare's milk.

(iv.) *Liqueurs* are strong spirits sweetened with sugar and flavoured with aromatic substances.

Curaçoa is flavoured with orange peel; Kirchwasser and Maraschino with cherries. The flavour of Chartreuse is complex, but is chiefly due to balm leaves and tops.

Absinthe is a bitter liqueur and is not drunk neat, as are the other liqueurs, but well diluted with water.

Liqueurs of British manufacture are usually inferior, and are known as cordials.

Bitters are a special kind of liqueur with tonic or medicinal properties. Gentian is the staple bitter.

Absinthe contains only 0·33 per cent of the oil of wormwood, which is responsible for its peculiar toxic effects, absolute alcohol 50 per cent, essential oils other than wormwood 2·5 per cent, sugar 1·5 per cent, water 45·65 per cent, and traces of chlorophyll. It has a convulsive action, stimulating not only the cortex, thus giving rise to epilepsy, but also the centres in the medulla; according to Boyce the cord is not affected by absinthe. The oil of wormwood exerts a direct toxic effect on the motor centres.

Chronic absinthism.—In these cases there are digestive disturbance, thirst, emaciation, loss of hair, tremor, giddiness, depression passing into melancholy or dementia, and, as already mentioned, epileptic fits which vary directly with the amount of the poison taken. "Absintheurs" suffer from hallucinations of hearing and sight quite apart from any condition like delirium tremens, and become utter wrecks physically and morally. The drug is chiefly drunk in Paris, where it was introduced after the Algerian war of 1844-47 by the soldiers who, when on service, had been advised to mix absinthe with their wine as a febrifuge.

(v.) *Other alcoholic solutions employed to produce intoxication.*—Ether is occasionally taken to induce intoxication, which is produced rapidly and by small quantities. [*Vide* art. on Ether Drinking, p. 909.]

Women have recourse to tincture of lavender, eau-de-cologne, and even tooth washes to satisfy their cravings for intoxication; and are thus enabled to drink secretly.

Tincture of capsicum, which has often been employed medicinally to overcome drink-craving, has also itself been used to produce drunkenness.

Jamaica ginger was so extensively consumed in Georgia (Dr. N. Kerr) that it has been scheduled there as an intoxicant. Its effects are said to be more depressing than those of alcohol alone.

ACUTE ALCOHOLISM

Drunken Fit.—The physiological effects of alcohol have already been referred to, and the ordinary phenomena of intoxication are too familiar to need much description.

As with other poisons or drugs, there is no constancy in the dose of alcohol which produces distinct results, or in the character of these effects in different persons. In some persons a small amount will produce most marked and violent intoxication; this is especially the case when there is a hereditary "alcoholic taint." The nervous system being unstable needs but little of the noxious poison—for such it is in these cases—to disturb its balance and to precipitate a condition which might be compared to temporary insanity. In cases where there is a family history of insanity the influence of the taint may show itself in maniacal excitement, in a suicidal or homicidal tendency, or in other imitations of recognised mental disease. This extreme susceptibility to the influence of alcohol may also depend on an acquired condition of nerve instability, such as follows a blow on the head or a sun-stroke. In the first stage of ordinary intoxication some functions of mental activity are increased, and imagination and thought are stimulated; but soon a want of self-control becomes evident, the silent man becomes confident and expansive, the habitually modest man boastful and egoistical; the restraint of reason is removed, and free play given to the expression of the feelings. As the clouding of the higher psychical centres concerned with thought, discrimination, and the control of the emotions advances, it spreads onwards to the motor areas; incoördination of ideas is succeeded by incoördination of speech and motion. Sometimes, however, the order may be reversed, and a person apparently sober so long as he is sitting down, may find on getting up that he is no longer master of his legs, and walks like a man with advanced locomotor ataxia. These effects of alcohol have been compared with those of advancing mental disease; general paralysis of the insane, with its progressive disintegration of the nervous system, being imitated by temporary intoxication. Dr. Maudsley describes drunkenness as a brief chronicle of the successive phases of insanity displayed in a short period of time. First there is a condition of stimulated energy with weakened self-control, like the mental excitement which often precedes mania; then follow motor and sensory disorders, incoherence of ideas, uncontrolled excitement or unreasoning melancholy; and, lastly, a condition of stupor which might be called temporary dementia.

When the full narcotic effect of alcohol has come about, the individual is, as it is commonly called, dead drunk. In this state of alcoholic coma the vaso-motor centre is paralysed, and, as a result of this, injuries which would kill a sober man by shock have comparatively little effect on the blissful or unconscious drunkard.

Acute alcoholic poisoning.—When a large quantity of strong spirit is taken at once—as, for instance, when a bottle of whisky or brandy is drunk off for a wager—the effect may be so extreme that death rapidly follows.

Such an event, however, is rare: it more often happens, when a quantity of strong spirit is taken, that considerable collapse from the irritating effect of the poison on the stomach walls comes on; then, as absorption takes place, the patient gradually passes into a state of coma like that which results when a large quantity of alcohol is imbibed gradually. This coma is due to the narcotic action of alcohol on the nerve-cells of the cerebral hemispheres. The unconsciousness is of varying degree; generally the patient can be roused by persistently tapping the forehead or slapping the face, or by the application of the battery. The limbs are flaccid, but there is no difference between the two sides, as in hemiplegia; the skin may be flushed and somewhat cyanosed, but is usually cold; the pupils are equal and generally dilated. The pulse is full, and the breathing deep and sometimes stertorous. The breath has an alcoholic odour, but little stress should be laid on this fact, as cerebral hæmorrhage or epilepsy may, of course, come on after drinking; or opium or other narcotic poisons, such as chloral, may have been mixed with the alcohol; or again, with the best intentions, friends or bystanders may have poured some stimulant into the patient's mouth after he began to be ill. Muscular twitching or general convulsions may occur, and these, if often repeated, may lead to the status epilepticus. If this occur the temperature may rise until death closes the scene, apparently from hyperpyrexia; still more rarely death, after an epileptic fit, may occur quite suddenly from syncope, with but little pyrexia. The occurrence of convulsions, however, is a comparatively infrequent event in acute alcoholic poisoning, the usual course being that of narcotic poisoning. The factors which in certain cases are responsible for these epileptic manifestations are—

(*a*) The existence of ordinary epilepsy in the patient, or of an hereditary taint; here drinking is one of many events which may precipitate an attack. (*b*) The convulsive action of certain alcoholic drinks; thus, absinthe and furfurol (which is found in spirit made from rye) give rise to a toxic epilepsy. Butylic and propylic alcohol have a similar convulsive action on animals, which ethylic or amylic alcohol do not possess.

In like manner it is the exception to find the temperature raised in alcoholic poisoning; as a rule it is depressed—sometimes to an extreme degree. If, however, the individual be inured to alcohol the depressing effect on the temperature is greatly diminished or absent. The coma may gradually deepen, and death from paralysis of the respiratory centre occur, or perhaps the patient may come round and then die somewhat suddenly. In the great majority of cases, however, appropriate treatment is followed by recovery.

Diagnosis.—With a clear account of the event there may be little doubt; but more often the diagnosis is one of probability only, and not infrequently it is impossible to be absolutely sure of the cause of coma in a person found in this state. In such circumstances the patient should be kept under careful supervision, and not left to sleep off a supposed drunken fit which may eventually turn out to be a state due to gross cerebral lesion.

Alcoholic coma may have to be diagnosed from post-epileptic states, from fracture of the skull, from intracranial hæmorrhage, from poisoning by narcotic poisons, and from the toxæmic coma of diabetes or of uræmia.

In distinguishing alcoholic coma from post-epileptic stupor the history and the condition of the tongue (whether bitten or not) will help. In cases where drinking has brought on an attack in an epileptic subject, the condition is one of epilepsy, and not necessarily of alcoholic poisoning —since a small amount of stimulant may produce this result; and the treatment should be directed accordingly.

Fractures of the skull may of course complicate drunkenness, and the coma may be due to depressed bone or meningeal hæmorrhage.

In cerebral hæmorrhage and in pontine hæmorrhage, pin-point pupils are usually present; the breathing is generally stertorous, but too much stress must not be laid on this. Dr. Bowles has insisted that stertor means no more than incipient suffocation in a comatose patient due to the supine posture; and that it can be stopped at once by turning him on his side. If doubt still exist it is wisest to wash the stomach out, and then treat the case as one of cerebral hæmorrhage. Even if the contents of the stomach smell of alcohol there may still be an intracranial lesion, since the excitement of a stimulant may be the immediate cause of cerebral hæmorrhage. The bladder if full should be emptied, as some valuable information may be derived from an examination of the urine. The presence of alcohol in the urine would point to the ingestion of a large quantity, and to the strong probability that the case is one of alcoholic poisoning. By the diazo reaction, as Dr. Hewlett has shown, minute traces of morphia (even 1 in 10,000) can be detected in the urine; in a doubtful case the use of this test might confirm or remove the suspicion of morphia poisoning. [But *vide* p. 893, note.—ED.] A considerable amount of albumin or sugar would point to uræmic or to diabetic coma; but it must be remembered that small quantities of either may be the result of intracranial lesions, and must not be confidently relied upon to indicate the cause of the symptoms.

Treatment.—In an ordinary case of drunkenness no special treatment is required; but when there is much stupor, or when coma is imminent, the stomach should be washed out by means of a soft rubber tube and funnel, and the patient roused by the application of the battery, or slapping with wet towels. When sufficiently awake, strong coffee may be given, and the patient put into a warm bed. Any signs of collapse must be treated by hot applications, friction, and, if need be, by a hypodermic injection of liquor strychninæ or ether.

Violent delirium or maniacal excitement may be rapidly subdued by the hypodermic injection of apomorphia, which is followed by vomiting and also by very considerable prostration. Convulsions, if recurrent, may be treated by the careful inhalation of chloroform, and the rare but dangerous pyrexia by the cold pack. As recovery proceeds gastritis will require appropriate treatment, which may with advantage begin with a sharp purge.

Morbid anatomy.—Congestion and acute inflammation of the stomach result from the irritating effect of strong spirit. The inflammatory process may go on to a superficial ulceration, but it does not usually pass beyond the catarrhal stage in which the mucous membrane is covered with ropy mucus.

The intestines and œsophagus have been described as showing a capillary injection of bright red colour.

Pulmonary "apoplexy" has been found in some cases. The brain has been described as having a distinctly alcoholic odour, but this is certainly not present in all cases.

Ætiology.—The causes of alcoholism may be divisible into the usual two headings:—(*a*) Predisposing; (*b*) Exciting. The former include the factors which are inherent in the individual himself, such as a special idiosyncrasy or susceptibility to alcohol due to hereditary causes, and also any acquired susceptibility such as may result from sun-stroke or injuries to the head. The influences exerted on the patient by his surroundings, profession, occupation, or trade are included under this head. Hereditary taint may be traced in a very large proportion of alcoholic cases—it is said in nearly a moiety. The children of drunkards are extremely susceptible to the influence of alcohol; a quantity that would not affect ordinary persons intoxicates them, and produces results not so readily seen in more normal persons. The crave for alcohol seems to be handed down to them, and they take to drink as a duck to water. It has been said that when the father has been a drunkard it is rather the moral nature of the offspring which is altered; when the taint is on the mother's side, that the brain and nerves are particularly liable to suffer: the mother's influence is said to be the more powerful of the two. Drunkenness not only breeds alcoholic tendencies but produces a decidedly neurotic taint and a strong predisposition to insanity; conversely, the offspring of neurotic or insane parents may be particularly susceptible to the effects of alcohol. Thus the influence of heredity consists in an unstable condition of the nervous system, which may be due either to drunkenness or to disorder of the nervous system in the parents. Thus drunkards beget "neuropaths" or "degenerates," and neuropaths again may have drunken offspring. Drunkenness has been divided into (*a*) simple or acquired, and (*b*) complicated or pathological; with the latter we are now dealing. The effect of alcohol is different in the two cases: a degenerate person suffers more severely and more rapidly. Thus he is more likely to die of delirium tremens, while an ordinary drunkard lives on, and eventually perhaps dies of cirrhosis of the liver. Not only does the degenerate person become affected earlier, and in a greater degree, but the manifestations are somewhat different, and are especially connected with the nervous system. Instead of the classical intoxication, a maniacal, melancholic, or suicidal drunken fit follows a debauch. Delirium tremens is more frequent; its stages are more prolonged, and are manifested more gradually than in ordinary drinkers. Impulsive drunkenness or dipsomania is the result of an hereditary taint, though it may come on when instability and loss of inhibitory power in the nerve-cells of the cortex have been acquired; as, for instance, after sun-stroke or head injuries. Such a sufferer, however healthy the stock of which he comes, after a blow on the head or a sun-stroke may become extremely susceptible to alcohol; just as if he were the offspring of drunkards or neurotics.

The influence of occupation is well marked. The liquor traffic naturally is pre-eminent as a hot-bed of intemperance. In the Collective Investigation Report, in fourteen occupation groups, the general percentage of hard drinkers was 15 per cent, and of free drinkers 15 per cent; while licensed victuallers showed a percentage of 43 per cent and 29 per cent respectively in the corresponding classes. Next, but long after, come trades necessitating exposure to severe weather—cabmen, drivers, night-watchmen, bargemen, and hawkers. Soldiers and domestic servants show a considerable degree of intemperance. Sailors, partly from force of circumstance, partly perhaps that their outdoor life counteracts the evil results of alcoholic excess, are, as a class, either more temperate or less poisoned than soldiers. The church has the post of honour in the list; among the other professions the schoolmasters approach most nearly to the ministers of religion, then officers in the army and navy, then medical men, and then lawyers.

Indoor occupations have been said to dispose to alcoholism from their dulness and monotony, and also because the effects of drink are not counteracted by active exercise in fresh air.

Apart from direct inheritance, the surroundings of the individual and the example of his parents will have a considerable influence, especially in the lower classes and in crowded populations. Race may be a factor of some importance. Dr. Norman Kerr (16) states that the Jews are very temperate; possibly this, and the care they take in selecting their food. accounts for their comparative freedom from tuberculosis. The inhabitants of cold or temperate countries are more addicted to alcoholic excesses than those of the tropical climates. The "Anglo-Saxon" race is considered by Dr. Kerr as being more prone to inebriety than any other; but, even if we do not look beyond Europe, the Russian is surely a severe competitor.

Increased prosperity of the country means an increased consumption of alcoholic liquors per head of the population; thus the consumption of beer per head, which was 24¼ gallons in 1861, and 29¼ in 1893, touched its highest point in 1874 at 34 gallons. In wines and spirits together the consumption per head in 1861 was 6⅞ pints, in 1875 10¼ pints, and in 1893 7⅞ pints per head. According to Sauerbeck's tables the average price of all commodities was higher in 1873 and in 1872 than in any of the years between 1825 and 1893. The average price of commodities may be taken as a general index of the prosperity of the country.

(*b*) Exciting causes.—Mental distress, loss of relations, friends, money, or reputation, drives many a sober man to the bottle. The desire to forget leads to much drinking, especially among women; and over-work, the desire to tide over a crisis, worry and its oft-accompanying sleeplessness, social gatherings, nay, even the wine of the Eucharist, may be the means of awakening a dormant taint or of sowing the seeds of the drink habit. Failing health, rheumatic or other pain, neuralgia, megrim, dyspepsia, menstrual troubles, or the disturbance of the menopause may act in the same way. Taken first as an anodyne, the habit grows and a definite craving becomes established. Dr. Isambard Owen, from the data of the Collective Investigation Report, estimated that one in every three of the population is liable, under appropriate conditions, to develop this morbid taste. The craving is rather for the after-effects than for the æsthetic pleasure experienced by the palate: the taste of the drink itself, indeed, is to some drunkards positively offensive. The means employed may be pleasant or repulsive; expensive wines, raw spirits, or whatsoever comes to the hand.

The morphia, cocaine and drink craves are much alike; from its ubiquity alcohol is the means most commonly employed, and once adopted is continued.

CHRONIC ALCOHOLISM

Chronic alcoholism is the condition which results from the toxic effects of long-continued alcoholic excesses on all the organs and tissues of the body, but especially on the nervous and digestive systems. It does not include the extreme results of the action of alcohol on particular organs—such as dementia, peripheral neuritis, or cirrhosis—but is the aggregate of the symptoms resulting from the earlier or preliminary stages of these and other morbid changes. The constant action of the poison leads to the establishment first of functional and later of structural alterations; and these two closely related factors are concerned in the symptoms of the disease known as chronic alcoholism.

From the continued activity of the temperance movement, and from the general belief that drinking habits, at any rate in the upper and middle classes, are much less than in past time, it might naturally be expected that alcoholism would be less frequent. Data for determining this point are difficult to obtain; but in so far as the death-rate from intemperance is an index of the existing frequency of alcoholism, this is not the case; indeed the reverse holds good. In the Registrar-General's Report for 1892 "the number of deaths ascribed to intemperance was 1971, being in the proportion of 67 per million living; the rates in 1890 and 1891 were rather higher, but with this exception the rate in 1892 was higher than in any previous year on record" (namely, to 1868). It is possible that this increase is rather apparent than real, and is due to the classification of such diseases as peripheral neuritis and hepatic cirrhosis, under the head of alcoholism; whereas formerly they were returned as paralysis and liver disease. W. Blyth points out that the recent rise in the death-rate of intemperance corresponds to a fall in that of liver diseases. The consumption of alcoholic drinks per head of the population has increased since 1856; in that year 22·6 gallons of beer and 1·26 gallons of wine and spirits were consumed per head of the population: in 1893 the amounts had increased to 29½ gallons and 1·35 gallons. In years of prosperity such as 1874, when 34 gallons of beer represented the consumption per head, and 1875, when 1·81 gallons of wine and spirits were taken, the amounts were much higher.

So far as statistics go, therefore, and they must not be pressed too far, there is reason to fear that alcoholism, although it appears to be diminished in some walks of life, is not really less frequent in one way or another than formerly. Secret drinking may have increased, or the frequent use of "nips," which does not bring about the grosser forms of drunkenness. The increase of wealth and luxury no doubt leads to a large use of alcohol as an element of "good living." On the other hand, the diminution of ordinary drinking is plain to every housekeeper and to every magistrate.[1]

Symptoms of the onset are gradual, and the patient probably does not seek medical advice until the malady is fairly well established.

In the early stages there is a disinclination to work and a general want of energy; so that, although routine occupation may be got through, it is not well done, and any additional exertion—physical or mental—is avoided. This malaise is succeeded by headache, low spirits, and a pervading sense of impending misfortune. The mental powers are weakened; there is indecision even in matters of little or no importance, irritability, and want of self-control: sleep fails, or is unrefreshing; and tremor, an early symptom, becomes manifest in the hands, lips and tongue. Anstie says that this tremor first occurs in the feet, and is worse in the morning, being chiefly due to the exhaustion of insomnia, and not entirely to the toxic effect of alcohol. To a certain extent, in the early stages, this tremor can be controlled by an effort of will; it is fine, and is brought out by any muscular effort, especially by an effort requiring precision or some slight manipulative skill. A sudden noise, such as the banging of a door, may make the patient tremble and perspire. There is, indeed, a general condition of jumpiness and nervousness—signs of a disordered cerebral function. The tremor is perhaps the first thing to attract the patient's attention, and to stop it he has recourse to an early morning dram; but food has a similar effect. These early symptoms persist and become more marked as the disease advances.

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[1] On this subject I may refer the reader to an article in the *National Review* for December 1895, by Dr. Shadwell, entitled "The Decline of Drunkenness."

In a well-developed case the features are probably flabby, and the face often shows signs of chronic venous congestion; this in the nose may pass into the well-known acne rosacea, well described by Trousseau, and still popularly regarded as "the indelible stigma of drunkenness." The inference is, however, by no means a necessary one; gutta rosacea may occur in uterine disturbance and in gastric catarrh due to causes other than alcohol. There is often some injection and slight œdema of the conjunctiva, and an icteric tint may be seen over the sclerotics. The skin of the body generally is smooth, soft, easily perspiring, and usually pale or even waxy. The tongue is usually, though not invariably, flabby and furred, and trembles when protruded; in women, however, the tongue is often clean, or it may be bare of epithelium. Superficial glossitis or leucoplakia may be found, especially in male alcoholics. The breath is foul, even apart from dyspepsia, and often has a peculiar heavy odour readily recognised by experienced observers; the mouth and throat are dry, and thirst is frequent. Pharyngitis and laryngitis of a chronic character are often met with, and lead to frequent hawking of phlegm and to some alteration of the voice. Want of appetite and indifference to food may pass into a positive loathing, so that very little nourishment is swallowed other than that which is contained in the alcoholic drinks. Like the other symptoms, the anorexia is worse in the morning; no breakfast is eaten, and a state of exhaustion follows, which drives its victim to seek support and relief in spirits or beer. This want of appetite is aggravated by morning nausea and sickness due to gastritis: a small quantity of yellow mucus is usually brought up, and the same condition of catarrh spreads, though in a less marked degree, to the intestines, and gives rise to the looseness of the bowels, which is a tell-tale symptom, and a capricious state of the intestines, in which constipation and diarrhœa alternate, is not uncommon. The gastro-intestinal symptoms vary considerably in intensity. Strong spirits are the most potent factors in the production of dyspepsia. Neat spirit is much more effective than larger quantities well diluted, inasmuch as its irritating action is more concentrated on the mucous membrane of the stomach. Occasionally the catarrhal gastritis of chronic drinkers may, as the result of a debauch, become quickened into an acute attack, and hæmatemesis may occur without there being any evidence, either at the time or subsequently, of cirrhosis of the liver.

Large draughts of beer may produce dilatation of the stomach and its accompanying symptoms. The liver in such cases is often tender and enlarged; a condition which may be due either to the early stages of cirrhosis, or to cardiac failure and consequent chronic venous congestion. Dr. Graham Steell has drawn attention to heart failure as a result of chronic alcoholism, and he points out that it is more often responsible for an enlarged and tender liver than is generally supposed; this hepatic condition may be erroneously regarded as an active congestion associated with cirrhosis.

Insomnia, which may have been present throughout, becomes worse, and is accompanied by nightmares and dreams of a terrifying and distressing character. In the dozing state between sleeping and waking startling hallucinations of sight or of hearing may further disturb the patient. They correspond to the *muscæ volitantes* — mists and clouds before the eyes, noises in the ears, and giddiness experienced in the daytime. Subjective peripheral sensations, numbness, tingling and cramps, or pain of a lancinating character, which appears to be neuralgic and gouty rather than the result of definite neuritis, may be met with; also starting and jumping of limbs, worse at night. The early symptoms of alcoholic peripheral neuritis are, of course, frequently present, but are not sufficiently conspicuous to stand out from the more general collection of symptoms known as chronic alcoholism.

Muscular tenderness, especially in the legs, alteration and impairment of sensation, pain, wasting and paresis of muscles, especially the extensors of the foot, leading to foot-drop, œdema, and loss of knee-jerk, may all occur and leave no doubt as to the existence of the lesions described under peripheral neuritis. [*Vide* special article.] Alcoholic neuritis begins and is best marked in the legs, affecting the extensors especially; but subsequently it spreads widely. It is rare for it to attack the cranial nerves, such as the ocular or facial nerves, in an isolated fashion; but in severe cases the vagus is probably not uncommonly affected, and may thus, by producing trophic degenerative changes in the myocardium, be responsible for cardiac disturbance and failure. Dr. Barlow has suggested that some cases of facial paralysis are alcoholic in origin, though unrecognised as such. Alcoholic neuritis is much commoner in women than in men—according to Dr. Gowers in the proportion of 3 to 1; and it often follows quiet and secret, though persistent, drinking. It may be that the greater outdoor activity of men in some way staves off the degeneration of peripheral nerves.

As the restlessness and nervousness grow worse, the depression of spirits may be so severe as to lead to suicidal attempts, or eventually to pass into melancholia. Want of will-power and lack of self-control are associated with failure in the memory, and form prominent features in the mental state of chronic alcoholism. There is a great alteration in the manner in which the items of the past and of the environment generally are regarded. Women suffering from alcoholic peripheral neuritis lose account of time, and are without the ordinary knowledge of their own whereabouts. A less marked form of this want of correlation with the outside world makes the chronic alcoholic absolutely untrustworthy and apparently a purposeless liar of the most unblushing kind.

Not only are the mental and the intellectual processes impaired, but there is blunting of the moral sense, so that falsehood and deceit, especially where indulgence in drink is concerned, become habitual and shameless. This is very commonly seen in women drinkers; and in men the loss of even these shreds of self-respect is shown in the cynical candour, albeit somewhat untruthful, with which they admit their past excesses, while, at the same time, they insist upon the recent reformation which, you must know, has come over their life.

The monotony of the course of chronic alcoholism may be varied from time to time by delirium tremens, or the local effects on some one tissue or organ may become predominant, and throw the general symptoms into the shade; so that the case now appears as one of cirrhosis, cardiac failure, peripheral neuritis, now passes into alcoholic dementia or other forms of definite mental disease.

Chronic alcoholism weakens the resistance of the body generally, and tends to favour the incidence of disease. It is notorious how badly alcoholics bear acute disease or injury. Thus pneumonia is generally admitted to be very fatal in drunkards, and its occurrence, or indeed, any other serious accident, such as a broken limb, is frequently associated with delirium. It is curious, however, that the Collective Investigation Committee, in their Report (13) upon the connection of disease with habits of intemperance, found that the mortality from pneumonia, and probably that from typhoid fever also, is not especially affected by alcoholic habits. This apparent contradiction may be partly explained by supposing that excessive drinking kills off its victims to the exclusion of other ordinary causes of death.

The prognosis of chronic alcoholism is not very hopeful. The craving for drink is extremely hard to eradicate; and, though it may be kept in abeyance for months or years, it will reassert itself when opportunity arises. The difficulty lies rather in reformation than in cure. The dyspepsia, tremor, sleeplessness, and so forth, can be alleviated with comparative ease so long as the patient is deprived of alcohol.

The occurrence of epilepsy is of bad omen. The prognosis will, of course, be much more serious in a long-standing case; when organic change has taken place in the brain, and dementia has resulted, recovery is highly improbable. However, in some cases of chronic alcoholism, even though structural change be present, the outlook is not so gloomy. Thus, in peripheral neuritis recovery is frequent; and even in cirrhosis of the liver improvement and perhaps partial recovery is, as Dr. Barlow has pointed out, by no means out of the question. On the whole, much depends on the success with which the drink crave can be combated. The immediate symptoms of the habit can usually be satisfactorily overcome; but a permanent and complete recovery is a matter of anxiety and uncertainty, and no case can be considered cured until at least two years have elapsed without any relapse into the habit.

Diagnosis.—Since chronic alcoholism manifests itself chiefly by nervous and digestive disorder, it may be simulated by the dyspepsia and accompanying nervousness which occur in failing health complicated by overwork or worry. A similar condition may be met with in women about the onset of the menopause, and in those who live on little more than strong tea.

The early stage of general paralysis of the insane may closely resemble chronic alcoholism; in both there is a progressive degeneration of the higher centres, an impairment of inhibition, and a loss of self-control leading to disordered action. If definite exaltation of ideas be present or the irresolute lip movements be persistent, there is no difficulty in the diagnosis; but there are cases of general paralysis in which the bodily symptoms are present without any mental alteration. In such cases signs of gastric disturbance, loss of appetite, morning sickness, and so forth, would point to chronic alcoholism. Alcoholism may, however, be a causal factor in the general paralysis of the insane. In the Fortieth Report of the Commissioners in Lunacy, 25 per cent of the male and 20 per cent of the female general paralytics were addicted to drink. Much lower estimates, however, are given; thus Dr. Savage found alcoholic excess but 7 times in 103 cases. Since drinking may be a symptom of the early stage of general paralysis, the two morbid states may be concurrent. Careful inquiry into the history and symptoms will be necessary to decide in such doubtful case.

The tremor of paralysis agitans and of disseminated sclerosis can be distinguished by their special characteristics from that of alcoholism.

The tremor of nervousness, hysteria, and senility may be mistaken for that of alcoholism; but further examination into the case will settle the diagnosis. Chronic alcoholism and tabes have several points of resemblance; the ataxic form of peripheral neuritis, as its name pseudotabes implies, may be confounded with locomotor ataxia. Gastric crises can usually be distinguished with ease from the gastritis and sickness of drinkers. The eye symptoms of tabes should always be looked for in considering the diagnosis of these two diseases.

The treatment consists in cutting the patient off from alcohol completely; but unfortunately the existence of the drink habit and craving render it very difficult to ensure this under the conditions of ordinary life. Even if the patient do his best, he is usually unable to withstand the besetting habit. Strong moral suasion and a full knowledge of the effects of the evil may perhaps keep him an abstainer for a time; but where temptation meets him at every other turn, as in everyday life it must almost necessarily do, it is almost too much to expect him to remain so.

Undoubtedly the best plan of treatment is for the patient to go into a licensed Retreat under the Inebriates Act (1888). At present a patient cannot be received against his will, however extreme his drunken habits may be. There is much to be said in favour of legislation which would assimilate the treatment of habitual drunkards to that of the insane; but the passing of such an Act might open the door to serious abuses. Having voluntarily entered a Retreat under the Act, the patient remains there for a definite term, and if he escapes during that period he can be brought back. Temptation is thus avoided in a way which is almost impossible elsewhere, and at the same time the inmate is under skilled medical treatment. The term of detention in the Retreat should never be less than six months; a year is necessary in ordinary cases, but in severe or inveterate cases a term of two years is desirable. Failing retirement to a Retreat, a long sea voyage on a ship or yacht from which all alcoholic drinks are excluded may be successful. Travelling with a total abstainer, preferably a medical man, or living in a private house where no stimulants are allowed, are other methods that may be adopted; but in none of them is there the same safety from temptation as that provided by a licensed retreat.

The first step is complete withdrawal of all alcoholic drink. This naturally has a marked effect on the patient, who at once feels the need of his accustomed stimulant. Depression, restlessness, and some degree of collapse may result; but experience shows that no harm follows from the sudden and complete removal of all stimulants. There is no proof of the old belief that delirium tremens can be thus precipitated. The patient should be carefully but unobtrusively watched after his arrival, and his strength sustained by simple food, peptonised if necessary. Feeding may be difficult from want of appetite, or from vomiting. Vomiting, Dr. Barlow points out, is far from being altogether an evil, as it removes tenacious mucus from the stomach, and so improves the conditions of digestion. The sickness should be treated by small quantities of liquid food, lime or soda water, alkalies, bismuth or effervescing mixtures, or by five minim doses of ipecacuanha wine. Sleeplessness should only be treated by sedatives if it is urgent. Morphia, chloral, and cocaine should be avoided lest the germs of a new craving be sown in the patient. Chloralamide, paraldehyde, trional, and bromides may be used if necessary; and the hypodermic injection of $\frac{1}{100}$ grain of hyoscine has been recommended. But before narcotics are employed, sleeplessness should first be combated by out-door exercise or fresh air, wet packs, or massage.

The bowels must be carefully attended to, and the appetite and digestion stimulated. Strychnia is very generally given, and abroad has been largely administered hypodermically; pepsin, bitters, tonics, and dilute acids are also of use. Much will depend on the way food is taken; as he improves the patient should get out a great deal, and should be well provided with suitable occupation.

Many drugs have been and are still used with a view of counteracting the craving for drink. Strychnia is often employed, and whether it have this special action or not, it certainly exerts a general tonic effect; tincture of capsicum in 5 to 10 minim doses has some effect in lessening taste for stimulants. It is well, however, to remember that it is an ic drink, and that it has been used as an intoxicant (8). Quinine, ona bark, atropine, aqua chlori, strophanthus, coca, and other also been recommended for this purpose.

Hypnotism has been employed with some success in creating a distaste for alcohol; while the patient is in one of the stages of the hypnotic state he is told that in future he will not be able to take alcohol: this is treatment by post-hypnotic suggestion. Its use has not met with much favour, chiefly from fear of abuse or because of its transient value. It should only be practised by a medical man, and in trustworthy hands is worth a trial. Its action is somewhat uncertain, but some apparently admirable results have been published.

Numerous "specifics" and patent "cures" have been vaunted; some of them appear to contain strychnia and atropine. An analysis of fifty different proprietary specifics showed that each contained alcohol in amounts varying from 6 to 47·5 per cent (27). It is not perhaps surprising that the condition of the patients is sometimes much worse after they have undergone these "cures."

Morbid anatomy.—*The Alimentary canal.*—Chronic congestion of the pharynx and pharyngitis are commonly met with. Chronic œsophagitis has been attributed to alcoholic excess.

Alcoholism is a frequent cause of chronic gastritis; the mucous membrane becomes thickened and fibrosed, and shows scattered areas of pigmentation, more especially in the region of the pylorus, due to chronic venous congestion. The gastric glands undergo degenerative changes, and eventually atrophy. The muscularis mucosæ and muscular coats may hypertrophy, and in extreme cases produce a contracted thick-walled organ—"cirrhosis" of the stomach. In beer drinkers the stomach may be greatly dilated. In acute alcoholic poisoning acute gastritis or, in rare cases, purulent gastritis may be produced.

Chronic congestion leading on to catarrh is common in the intestines, but there are no very manifest naked-eye lesions in the intestines directly due to alcoholism.

Piles, whether due to former constipation or concomitant cirrhosis, may be made to bleed, and have been known to become extremely irritable after alcohol has been taken.

It has been stated that chronic pancreatitis may be caused by alcoholism.

Liver.—Cirrhosis of the liver is far more often due to alcoholic excess than to any other cause. In sixty-seven cases of cirrhosis analysed by the Collective Investigation Committee 60 per cent were described as hard drinkers, 30 per cent as free drinkers, none was a teetotaller, and 10 per cent only were fairly temperate. Dr. Dickinson (8) found that cirrhosis was present eight times in the bodies of 149 persons who were not in any special way connected with the liquor trade; and that in 149 traders in alcohol, cirrhosis was present twenty-two times. It is noteworthy that, although alcohol is the main cause of cirrhosis, it is by no means so common for cirrhosis to occur in the course of chronic alcoholism. Thus Formad, in 250 post-mortems on confirmed drunkards who had died suddenly from the effect of alcohol, only found cirrhosis in six, and concluded from this that alcohol does not produce cirrhosis.

Possibly the contrast between the frequency with which alcoholism figures in the history of cirrhosis, and the percentage of cirrhosis in confirmed drunkards, may be explained by supposing that when in any patient the liver is susceptible and likely to suffer from the action of alcohol, it becomes affected comparatively quickly; and that, before the clinical picture of chronic alcoholism has had time to be completed, the symptoms of hepatic cirrhosis have become clearly outlined.

The statement that cirrhosis may follow prolonged exposure merely to alcoholic fumes apart from any consumption of the liquor is very difficult to prove.

The cirrhosis may be associated with fatty change in the hepatic cells; thus the large liver is produced, which is found when the patient has been a high feeder, and when malted or sugary beverages have been taken. The atrophic form, in which the cells are compressed and atrophied, and contain little or no fat, often, though not invariably, follows the use of spirits, as is implied by its names gin or whisky drinker's liver. In addition to the usual microscopic appearances of atrophic and mixed (fibrous and fatty) cirrhosis, those considered to be characteristic of biliary cirrhosis, that is, the formation of new bile-ducts; may be present.

It has generally been supposed that the alcohol, by setting up inflammatory changes in the connective tissue of the portal canals, leads to the formation of new fibrous tissue which compresses the liver-cells, and thus produces atrophy of them. It is probable, however, that the morbid processes in cirrhosis are not limited to the formation of inflammatory tissue, but that atrophy of the hepatic cells and proliferation of the interstitial connective tissue occur simultaneously, and are due to the same cause. The view that the degenerative change in the cellular or active part of the organ is, as in alcoholic neuritis, the all-important factor, and that the fibrosis is a passive overgrowth, or of the nature of the fibrous substitution that occurs in old age, has been put forward; but it does not seem to be borne out by the histological appearances, which undoubtedly show an active formation of young connective tissue. From the direct action of alcohol on the cells, however, degenerative changes result. Extensive fatty changes (steatosis) are common in drinkers apart from cirrhosis. Dr. Payne has suggested that an extremely rare condition—acute red atrophy of the liver, in which the liver-cells are in an advanced state of degeneration and necrosis, is due to alcoholic excess.

Alcoholic cirrhosis is very frequently associated with tubercle elsewhere. Thus in 75 cases of tuberculosis in alcoholic subjects there was cirrhosis in 46 or 60 per cent (Mackenzie). It is probable that alcoholic cirrhosis is less frequent in persons who lead an active out-door existence.

Kidneys.—The amount of alcohol traversing the kidneys is probably small compared with that which passes through the liver. Since, however, it is a tissue poison, we may expect that the delicate renal epithelium, in common with the brain and nerves, would suffer from its toxic action. It is possible that in this way transitory albuminuria following excessive drinking is explained. Some degree of fatty degeneration of the renal epithelium is common in drunkards, but the continued action of alcohol does not appear to be followed by an overgrowth of fibrous tissue secondary to the degeneration of the active functional parts of the kidney, such as we find in the cord in "lateral sclerosis," and in the kidney itself in old age. Thus Dr. Dickinson (8) found granular kidney nearly in the same proportion in two series of 149 patients, one series being made up of patients who were connected with the liquor traffic, and so presumably drinkers, and the other series composed of persons who were not drunkards, or brought in contact in any especial way with alcohol. In the liquor traders granular kidney occurred 31, and in the control cases 27 times. Formad, in 250 sudden deaths occurring in confirmed drinkers, found Bright's disease in 25, and concluded from this that there is no causal relation between drinking and kidney disease. It is, of course, possible that hard drinkers are enabled to carry on the practice in virtue of a comparative general immunity to the toxic action of alcohol; and the fact that Formad only found cirrhosis of the liver six times in these cases supports this hypothesis. That confirmed drunkards do not show signs of kidney disease does not necessarily prove that alcohol may not affect the kidneys in more susceptible persons; the toxic results in such cases might be so marked as to prevent the individual from drinking to excess. But Dickinson's statistics show that granular kidney has little claim to be considered as the result of alcoholism.

It has been alleged that alcoholism affects the kidneys indirectly—that it first leads to gout and arterial change, and so to the kidney of arterio-sclerosis. In Formad's cases the kidneys were swollen and two ounces in excess of their normal weight. Dr. Pitt in 89 cases of hepatic cirrhosis, with marked alcoholic history, found that the kidneys weighed over 10 oz. in 38, and over 15 oz. in 16 instances. These large kidneys showed little or no structural change, and appeared to be hypertrophied from increased function; as may be the case in diabetes.

The question of the effect of alcohol on the kidneys is not completely answered; but it appears that there is no positive evidence that grave lesions in any degree comparable to cirrhosis of the liver are thus produced.

Relation of cirrhosis of the liver to kidney disease.—In his 89 cases of alcoholic cirrhosis Dr. Pitt found 18 cases of granular kidney and five of tubal nephritis. In 60 cases of cirrhosis, collected from St. George's Hospital post-mortem books, there were five cases of chronic interstitial, and one each of chronic parenchymatous and lardaceous disease.

Dr. Dickinson found cirrhosis of the liver, in cases of granular kidney, in the proportion of 1 in 7; and concluded that, though both liver and kidney are exceedingly liable to fibrosis, they seldom become fibrotic together; and that the change in the two organs respectively is due to different morbid agencies (9).

Respiratory organs.—Alcohol is excreted by the lungs to some extent. The direct toxic action exerted by it on the mucous membrane is probably the cause of the bronchial catarrh which is not uncommon in drinkers.

Chronic laryngitis with thickening and opacity of the mucosa, which becomes like the epidermis (pachydermia laryngitis), may occur in drunkards.

The old notion that alcoholism is protective against the development of tuberculosis is the reverse of the truth. Dickinson (9) found pulmonary tuberculosis to be more frequent in drinkers than in ordinary people, in the proportion of 3 to 2. Dr. H. Mackenzie, in 67 cases of pulmonary tuberculosis occurring in drinkers, found a family history of tubercle in 10 only. Since a family history of the disease is present in about 30 per cent of the ordinary cases, the effect of alcohol in producing pulmonary tuberculosis is considerable.

Pulmonary tuberculosis of an active type is very frequent in peripheral neuritis of alcoholic origin, and has been regarded as "trophic," and due to changes in the vagi. Such a factor may have had some share in the result; but the generally debilitating influence of alcoholism is probably more important. With other forms of peripheral neuritis, with the exception of leprosy, pulmonary tuberculosis is not often coincident.

Tubercles in the lungs are frequently found post-mortem in cases of cirrhosis of the liver, which disease in the great majority of instances is of alcoholic origin. In 122 cases of cirrhosis, quoted by Pitt, tubercular lesions in the lungs occurred in 30·9 per cent. There were old cavities with fibroid change at the apices, and almost invariably a general dissemination of gray tubercles in the lungs. Of Dr. H. Mackenzie's cases of tuberculosis in heavy drinkers there was cirrhosis of the liver in more than one-half; in 100 consecutive cases of fatal phthisis occurring in persons over 20 years of age, in the last four years at St. George's Hospital, cirrhosis of the liver in any degree was present but 12 times.

In his cases of alcoholic pulmonary tuberculosis Dr. H. Mackenzie observed excavation with bronchopneumonic consolidation and gray tubercles. The cases ran a rapid course. Fibroid tubercle was comparatively rare; but it must be remembered that these were clinically cases of tuberculosis, and this observation does not clash with the fact that very chronic pulmonary tuberculosis is commonly present in the bodies of drinkers.

Nervous system.—Thickenings of the pia mater and arachnoid, increase in size of the Pacchionian bodies, and excess of the subarachnoid fluid due to atrophy of the brain, are common in alcoholic subjects, but are also normally found in old persons. In some rather exceptional cases pachymeningitis has been found; and not unfrequently there are signs of chronic meningitis, such as thickening of the pia mater and adhesion to the underlying cortex. The brain is shrunken, and the convolutions distinctly separated by the sulci. The ependyma of the ventricles has been described as granular or villous, as in general paralysis of the insane. Microscopically the vessels passing in from the pia mater, and those in the brain substance, are tortuous, and show endarteritis and miliary aneurysms. The perivascular lymph spaces are dilated.

Degener [illegible] with on the fifth layer of the motor cells of the vortex (Bevan Lewis). The cells become vacuolated, undergo fatty degeneration from the toxic effect of alcohol, and finally disappear. The "spider cells" are greatly increased in number, and form cicatricial tissue. These effects are comparable to those occurring in the interstitial hepatitis.

Chronic myelitis, probably due to meningitis and not showing any systemic arrangement, is met with. This may occur as the result of injuries so slight that but for the accessory element of alcoholism no change would have occurred in the cord (12). The condition may be associated with neuritis, but is independent of it. There is increased vascularity, most marked in the posterior columns, and increased numbers of the spider cells.

Degenerative changes occur irregularly in various groups of the ganglion cells of the cord.

Systemic scleroses in the cord are occasionally seen, and when in the ascending tracts might be attributed to neuritis or an extension of the same process. Bevan Lewis, however, considers this by no means probable, and says the cord changes are due to slowly encroaching sclerous changes spreading from the membranes and creeping along the vascular tracts, especially along the posterior median raphe.

Optic neuritis in alcoholic subjects may be due to chronic meningitis. Dr. Sharkey (30) has recorded a case of alcoholic retinitis.

The changes on the nerves begin near their peripheral distribution, especially in the intramuscular branches of the motor nerves. Dr. Sidney Martin has described the following changes:—First at one or more spots on a nerve fibre the medullary sheath disappears entirely, the remainder of the sheath above and below this interruption still staining with osmic acid; the axis cylinder in the affected part becomes attenuated and finally ruptures. The part of the nerve fibre between the rupture and the muscle now undergoes Wallerian degeneration. The process is, therefore, primarily one of peripheral nerve poisoning and degeneration, and not of neuritis in the ordinary acceptance of that term. Sharkey (31) has, however, figured acute inflammatory changes in the phrenic and vagus in alcoholic neuritis.

The degenerative effects of alcohol are developed more rapidly in the peripheral than in the central nervous system. Recovery occurs in peripheral neuritis, but when there is reason to believe that definite organic change has taken place in the brain the prognosis is very bad.

Heart and Vessels.—Neuritis of the vagus as suggested by Sharkey (30) probably leads to fatty degeneration of the myocardium, and must play an important part in cardiac dilatation occurring in alcoholism. Moreover the direct action of alcohol on the heart muscles tends to enfeeble its contractile power. In the heart failure in alcoholism, the clinical features of which Dr. Graham Steell has described, the heart is dilated and presents compensatory hypertrophy; it may weigh as much as 24 oz. Aufrecht describes the lesion as one of chronic interstitial myocarditis.

The alcoholic heart resembles a dilated heart due to chronic interstitial nephritis; while at the same time the kidneys show the effects of chronic venous congestion. The association of cardiac kidneys and renal heart had puzzled pathologists before Graham Steell's admirable paper threw light on the causation of these events.

As elsewhere in the body fatty infiltration under the visceral pericardium may be excessive.

Alcohol is usually said to produce atheroma of the larger arteries, and in the same way to lead to sclerotic changes in the valves of the heart, and so to valvular disease. Chronic endarteritis of the aorta may spread to the aortic valves and produce incompetency or stenosis.

The effect of alcohol on the arterioles is compared by Bevan Lewis to that of chronic interstitial nephritis; and probably the same factors—a toxic condition of the blood—are present in both.

Indirectly alcoholism produces changes in the veins: thus cardiac failure and the resulting chronic venous congestion lead to dilated and varicose veins, and gout to thrombosis.

The Generative organs.—The testes have been described as much atrophied in drunkards, but this event is very exceptional, and may have been an accidental association. Lancereaux has described an alteration in the seminal tubes of the nature of a premature senile change. Chronic alcoholism appears to diminish the fertility of both sexes, and to lead to a stunted and ill-developed offspring. In women it has been thought that this is brought about by interstitial changes leading to fibrosis of the ovaries. Although every variety of menstrual disorder may occur, menorrhagia, possibly due to endometritis of the body of the uterus, is by far the most common (20).

The skin becomes very smooth, waxy-looking, and extremely soft to the touch; this is partly due to the accumulation of fat under the skin, and partly to atrophy of the skin.

Chronic venous congestion of the face and acne rosacea are often, though by no means invariably, due to alcoholic excess.

The muscles of the body appear flabby and somewhat fatty. In peripheral neuritis Dr. Sharkey (30) has described active inflammatory changes occurring in the paralysed muscles.

Bones and Joints.—The bones, like the rest of the body, are said to show an increase in the amount of fat.

Alcoholic drinks have no influence on osteo-arthritis.

By producing gout alcohol affects the joints in a marked though indirect way. The stronger wines—Port, Sherry, Madeira—and heavy beer and porter are most powerful gout-inducing agents. Burgundy is very badly borne by gouty patients. Champagne differs in its effects, the dry brands being less harmful than the sweet. Claret, Hock, Moselle and the lighter forms of malt liquors have comparatively slight gout-producing tendencies. Sir A. Garrod says that neither the acid, the sugar, nor any known principle in alcoholic drinks can be shown to be the active factor in producing gout. According to Dr. Haig, a liquor is harmful in proportion as it tends to diminish the alkalinity of the blood.

DELIRIUM TREMENS

(SYN.—Alcoholic delirium, "The Horrors")

Introduction — Symptoms — Diagnosis — Prognosis — Treatment — Morbid Anatomy—Acute Alcoholic Insanity—Dipsomania.

Though often described as acute alcoholism, and sometimes coming on after a single bout of hard drinking, delirium tremens is usually an exacerbation in the course of chronic alcoholism occurring in constant soakers who are rarely drunk but hardly ever sober.

An hereditary taint, whether of insanity, alcoholism, or other neurosis, increases the liability to delirium tremens. This is probably the determining factor in many cases where the symptoms have arisen acutely after a single debauch in a person not an habitual drunkard. The unstable condition of brain matter which is acquired by long-continued alcoholic excess in other cases is hereditary in the neuropath, and in the offspring of drunkards.

It was formerly supposed that delirium tremens was often caused by the interruption of the drinker's accustomed alcoholic stimulus. But the fact is that the distaste for drink is the beginning, and one of the earliest symptoms of an impending attack of delirium tremens—the result and not the cause of the disease. The attack, indeed, is often brought on by a bout of harder drinking than usual.

A severe injury, a sudden shock, mental or bodily, or the onset of acute disease, especially pneumonia, may in a constant drinker bring on the symptoms of delirium. After operations this form of delirium may occur; but it is practically unknown in childbirth, though it occasionally follows uterine operations. This state has been called "associated delirium" (Gowers), or "traumatic delirium" (S. West), and is dependent on two factors, (*a*) the long-continued toxic effects of alcohol, and (*b*) the depressing effect of injury or disease; so that, other things being equal, the prognosis is not so good in this form of delirium as in delirium tremens. Indeed, in ordinary cases of the disease there is often some minor exciting cause which acts as a "last straw" in the case of a soaker on the verge of delirium tremens; thus there are transitional stages between the classical form of delirium tremens and that which appears to be precipitated by momentary accident.

Delirium tremens seems to have been first recognised as a symptom group, and separated from acute mania, by Dr. Thomas Sutton of Greenwich in 1813; and to have been most accurately described by Dr. John Ware of Boston, U.S.A., in 1831.

Symptoms.—In the premonitory stage, which is of variable duration, there is increasing restlessness and nervousness. Appetite for food is lost, and often even the taste for alcohol fails, or is turned to loathing; on the other hand, drinking may be continued right up to the full onset of severe symptoms. The night brings no real rest or refreshment, and passing slumbers are disturbed or broken by unpleasant or terrific dreams. Hallucinations crowd into the waking moments, and begin to be troublesome also in the daytime; but at first they may be diverted or even dismissed by an effort of will.

The onset of the actual delirium in the second stage is indicated by an exaggeration of these symptoms. Tremor is a marked feature, and, though it is more manifest in the hands, tongue, and lips, it is only necessary to lay a hand on the patient's shoulder in order to detect vibrations all over him. This tremor is a further development of that of chronic alcoholism, and is part of a great and indeed universal muscular unrest which shows itself in continued though ineffectual activity. The tendons of the patient's fingers and the hands are continually at work, repeating the habitual manipulations of his trade or occupation, ceaselessly pulling up and picking at the bed-clothes, or scratching the body; he fidgets perpetually, and never rests. At times the sufferer wriggles under the clothes like an imprisoned animal. The mind is active enough, and is engaged in making plans for the future; or is swept into the whirl of hallucinations which can no longer be dismissed. The delirium is busy with a continual succession of ever-changing ideas, but each train of thought lasts for a short time only. A general uneasiness and a desire to move on possess the patient; he would pack up, start on a journey, or, as Trousseau expresses it, get away from himself. The activity of his mental processes is incontinently expressed by garrulous and incoherent talk, concerned chiefly with the figments of his brain; though surrounding circumstances come in for some contemptuous or querulous comments. Yet for a time, even in the midst of his multitudinous and imaginary pursuits, he can collect himself sufficiently to answer simple questions appositely. The face is anxious, the skin bathed in perspiration, the eyes furtive and perpetually-moving, and the pupils usually dilated. The excitement is due to fear, engendered by delusions and by the visual and aural hallucinations. These are nearly always loathsome or terrifying—such as beetles, swarms of rats, fishes in the bed, horses' heads thrust through the walls, or yet more formidable creations of a morbid imagination. Later he ceases to recognise those around him, he sees in his friends or attendants designing enemies or derisive fiends, and fancies that insults and offensive remarks emanate from them, or that they are attempting to poison him or to feed him with offensive food.

The prevailing note of the delirium is one of terror: in order to escape, the patient is ever anxious to be up and off, and, if at liberty, would make an immediate exit without ceremony or dressing; sometimes indeed by the bedroom window instead of the door. He is suspicious, ever on the watch for some horrible object concealed behind the curtains of the bed or lurking in a corner of the room. Occasionally, under some hallucination, he may attack the attendants; but generally he can be controlled or humoured with tact. The pulse is now rapid and soft, the tongue moist, tremulous, and covered with creamy fur. The temperature is usually raised, in mild cases to 100° or 101°, and in severe cases to 103°, with no local lesion to account for it; though the apprehension of a latent pneumonia must never escape the mind of the physician. There is complete insomnia and absence of appetite.

The disease, as Dr. Ware pointed out, is self-limiting; and after two and a half, three, or four days, the acute stage, in most cases, undergoes a spontaneous amelioration. The patient, who has suffered from absolute insomnia, sinks into a quiet, refreshing sleep, and when he awakes is free from the delirium and hallucinations; though he does not lose the tremor for some time. In favourable cases convalescence is rapid. In severe cases, especially when there have been several previous attacks, the temperature may rise and fatal hyperpyrexia result; or again, pneumonia may set in; or the delirium may continue, and the patient pass into a low typhoid state; or collapse or death from syncope may suddenly close the scene. In other cases, again, the delirium may continue and signs of general failure supervene. Sometimes epileptic seizures come on, which are of very grave import.

Diagnosis.—Acute mania is the disease most likely to be confounded with delirium tremens; but the tremor, the special character of the hallucinations, and the behaviour of the patient, will distinguish the latter from the former. To general paralysis of the brain with tremor there is some resemblance; but the mental exaltation of the excited stages of general paralysis should distinguish these patients at once from the terrified subjects of delirium tremens.

The question of diagnosis between meningitis and other forms of organic brain disease and delirium tremens does not often arise, though it appears to have arisen in former times; the presence of paralysis, severe headache, optic neuritis, uneven pulse, and oppression of consciousness point to organic brain lesion; while the presence of the characteristic delirium and tremor would at once suggest delirium tremens.

In fevers, such as typhoid, where delirium may form part of the disease quite apart from alcoholism, it may at a given moment be difficult to decide whether the delirium be symptomatic—that is, due to the specific fever, or whether it be the form of delirium tremens ("associated delirium") which supervenes when injury or acute disease befalls a drunkard. The important condition, however, in this case is not the delirium, but the primary disease.

For the diagnosis between delirium tremens due to alcohol and the similar delirium due to withdrawal of morphia from the morphinist, the reader is referred to the article on Morphinism in this volume.

Prognosis.—In first and uncomplicated attacks recovery is very general, though in a chronic alcoholic recurrence is extremely probable. Old age, previous attacks, and the presence of complications or other morbid conditions, render the disease a formidable one.

In "associated delirium" the nervous system is suffering on the one hand from shock due to the injury or disease, and on the other from the long-continued effects of alcohol; the prognosis is therefore worse than in ordinary cases of delirium tremens. Much, of course, depends on the character of the injury or acute disease; in pneumonia a drinker's chance of recovery is poor, and double pneumonia is practically always fatal.

The state of the heart is of primary importance. A heart already dilated is a very serious condition. Signs of approaching cardiac failure —such as faintness, a small, irregular, very frequent (over 130) or running pulse, a soft, feeble, or inaudible first sound, or a murmur at the apex with an accentuated second sound at the right base—are of very bad omen.

Pre-existing kidney disease is a grave condition, as uræmia may supervene.

If pneumonia appear in the course of the disease the outlook becomes very anxious. A temperature of about 103°, especially in old and debilitated subjects, is always a cause of grave anxiety; it may be due to the insidious establishment of pneumonia, or it may be merely an index of the proposed functional disturbance. Hyperpyrexia is usually fatal.

Convulsions in the early stage, according to Gowers, are not of much importance; but when they occur later the prognosis becomes very grave.

A patient who takes and digests his food usually does well; while cirrhosis of the liver or gastric catarrh, by interfering with digestion, diminishes the patient's chances of recovery. If the disease run on and sleep be not obtained, or obtained only in very insufficient amounts, there is great danger of exhaustion.

On amendment the symptoms may only partially abate and a condition of mental enfeeblement may persist. After repeated attacks some degree of weak-mindedness is often permanent.

There are then three degrees of the disease:—

(i.) Uncomplicated attacks, in which the prognosis is good;

(ii.) Associated delirium, in which the prognosis depends largely on the severity of the affection exciting the delirium; and

(iii.) Cases complicated by old age, debility, previous attacks, or the presence of visceral disease, in all which the prognosis is very bad.

Treatment.—The most important points are food, sleep, management, and restraint.

Feeding is of great importance, seeing that the patient is in a half-starved condition, and, as a rule, has taken little food for a considerable time before the onset of acute symptoms. Careful feeding from the outset is very important, both for immediate relief and to prevent exhaustion and cardiac failure in the later stages of the disease.

Anorexia and unwillingness to take food (which may be due to a delusion that it is poisonous, disgusting, or offensive) require considerable tact and good-nature on the part of the attendants. If necessary a nasal tube should be passed and fluid food thus introduced into the [illegible] not more than three hours.

Beef-tea, peptonised milk, soups or broths, and, if acceptable, pounded fish or mincemeat, should be given. Care should be taken, however, not to overload a stomach the digestive powers of which are almost certainly much impaired by chronic catarrh. Vomiting must be combated by ice, effervescing draughts, lime water, and careful feeding with small quantities; if it persist, nutrient enemas or suppositories must be employed. Stimulants should only be given in the presence of severe complications, such as cardiac failure, pneumonia, or great exhaustion. Ether and ammonia, brandy, whisky, or old port should then be given by the mouth; but absorption is slow, and if the symptoms continue, hypodermic injections of liquor strychninæ ♏ ij., ether, or brandy are indicated. It is probable that these are the cases most likely to be benefited by the large doses of digitalis (half an ounce of the tincture) formerly employed by Mr. Jones of Jersey.

A brisk purge should be given at the beginning of the attack, and repeated if the tongue be foul or constipation be present.

In pneumonia inhalation of oxygen may be necessary.

Sleep.—The disease, as was shown by Dr. Ware, tends to run a definite course. In favourable cases the acute stage terminates in sleep, after which the patient is no longer delirious. Probably as a result of this sequence of events, the belief arose that to cure delirium tremens the proper treatment is to send the patient to sleep. Sir T. Watson expressed this view of the treatment in his Lectures on Physic with no uncertain voice. For this purpose morphia or opium was largely given; in many cases the drugs failed to produce any effect for a considerable time, probably owing to delay in the absorption from the stomach. In this case large doses of opium were sometimes repeated, and with the result that the sleep-at-any-price treatment tended rather to substitute narcotic for alcoholic poisoning than to cure the patient. Instances of fatal results directly due to the "narcotic treatment" are not by any means unknown. On the other hand, the "natural" method of treatment aimed at giving no narcotics in ordinary cases, and letting the disease run its course. In prolonged sleeplessness, however, moderate doses of opium were given. Care is necessary, not only in deciding when measures to ensure sleep should be taken, but also in deciding on the means to be employed for this end.

Hypodermic injection is a very much more certain method of administering narcotics than by the mouth; hence morphia is more convenient than opium. After an injection has been given, the effect on the pupils should be watched and a second injection should not be given until the effect of the first has begun to wear off; so as to avoid any possibility of narcotic poisoning. If the dose of morphia or opium have no sedative effect on the nervous system, it should not be repeated, as there is then some danger of its acting as a cardiac depressant (Anstie). Osler speaks well of hyoscine in $\frac{1}{100}$th gr. dose hypodermically.

Chloral was employed successfully by Anstie. It has a depressing action on the heart, and must not be used without careful examination of that organ. Chloralamide, sulphonal, and paraldehyde are safer and often effective (Gowers). Bromides have had an extensive trial, but with no great success.

It has been suggested that a pint of bitter beer or porter may be the best hypnotic in delirium tremens; this may be the case, but, as the use of alcohol tends to keep up the drink crave, the use of it is to be avoided if possible.

Hot and cold packs have been highly recommended as a means of inducing sleep.

Acting on the belief that delirium tremens is due to the cumulative effects of alcohol, Dr. Peddie gave antimony in order to assist in its elimination, and Dr. Norman Kerr (14) prescribes liquor ammoniæ acetatis with the same object.

The best course is not to give hypnotics unless the case be prolonged, or it appears that the patient, wearing out his strength, is in danger of exhaustion. Then, unless there be any marked contra-indication, such as severe lung or kidney mischief, morphia should be given hypodermically. If morphia be undesirable, a trial should be made of sulphonal, paraldehyde, chloralamide, or chloral; combined, if need be, with a cold or hot pack.

Restraint and general management.—Constant watching is of great importance; in the acute stage the patient, if left alone for a moment, may jump out of the window, or commit suicide in a most determined manner. Two strong nurses should be in attendance, and should never quit the room for an instant until relieved.

The patient should be placed in a cool, quiet, and dark room, so as to favour the advent of sleep; and should lie on a low bed preferably padded—beds with sides of woven wire are now made, and are very useful—or on a mattress on the floor of a padded room. No mechanical restraint must be used unless the difficulties be exceptionally great, or the staff of attendants weak. If two attendants be insufficient, the number must be increased. In the presence of a sufficient number of attendants accustomed to the management of such cases, mechanical restraint is not needed. All such patients are quick enough to see their moments for submission or for escape. If mechanical restraint be absolutely necessary, a strong sheet may be tucked well and tightly down on both sides, but no straps or folds across the body are permissible, as such bands arrest respiration, if they do not now and then break a rib. Strait-jackets are a survival of the dark ages, and leather wrist-bands and bandages abrade the skin and give rise to sores. An attendant who kneels upon a patient must be instantly dismissed.

Very much can be done without any restraint by attendants who know how to humour the patient, and have tact in soothing and diverting him.

As convalescence advances attempts to overcome the drink habit should be made by moral suasion, and by the administration of nux vomica, capsicum, and the like. After recovery the patient may with advantage go into a licensed Retreat under the Inebriates Acts, in order if possible to be cured of the drink habit. [*Vide* Treatment of Chronic Alcoholism.]

Morbid Anatomy.—In fatal cases of delirium tremens the general lesions of chronic alcoholism may be found after death, as might be expected from the fact that the delirium is so frequently an exacerbation of that disease.

The kidneys are usually large, and present the hypertrophy due to an increased functional activity. The liver is fatty and often much increased in weight from this cause.

Inasmuch as death is usually due to cardiac failure the heart is flabby, somewhat dilated, and often shows some fatty degeneration of the myocardium (tabby-cat striation).

From the manner of death hypostatic congestion of the lungs is commonly to be expected.

For other morbid changes the reader is referred to Chronic Alcoholism.

Acute Alcoholic Mania and Melancholia.—In persons with an hereditary nervous irritability alcoholic excess may be the immediate cause of an outburst of acute mania or melancholia.

Alcohol is thus, by accident as it were, the exciting cause of an attack of acute mental aberration; but the symptoms may not be in any way characteristic of alcoholism. This subject is therefore part of the section on insanity, and will not be further treated here.

Dipsomania.—Dipsomania or oinomania is a form of recurrent mania attended with impulsive drunkenness. It occurs periodically at intervals of two to twelve months in persons who at other times are perfectly sober and free from the drink crave. It attacks only those who have a decidedly hereditary taint, or who have acquired a certain instability of the nervous system from head injuries, sun-stroke, and the like.

In women the periodic outbreak often, but by no means always, coincides with the menstrual flow.

The premonitory symptoms are restlessness and irritability of body and mind, sleeplessness, and mental depression and change in conduct. After ineffectual struggles the barriers of self-control break down, often towards night or in the night; alcohol in some form is taken copiously, and the patient may then drink straight on, and be continuously drunk for a week or a fortnight; or he may impulsively drain a decanter of wine, and rise in the morning released from temptation.

When the outbreak has been a disgraceful one the sinner is overcome with grief and shame, and pursues the tenor of a sober and regular life until the next periodic attack causes him again to run amok in alcohol.

In dipsomania, between the recurrent attacks there is no drink crave and no great danger from temptation; it thus differs from chronic alcoholism. It is doubtful whether it can ever be cured, though the attacks may for a lifetime be so brief as to remain unknown to the world. In those cases in which one heavy draught suffices to allay the craving, there is often indeed no apparent intoxication, an immunity we may occasionally observe in persons who drink deeply during violent neuralgia: the dose seems to be expended on the restoration of equilibrium.

Dipsomania evidently belongs rather to insanity than to alcoholism.

H. D. ROLLESTON.

Postscript.—Patients may be admitted into licensed Retreats either under the Inebriates Acts, 1879, 1888, or privately (not under the Acts); in the latter case they must conform to the regulations which bind the patients under the Acts: but they can, with the approval of their friends, leave the Retreat when they see fit. If proceeding under the Acts, the patient must sign the request for admission (*vide* below) into a Retreat in the presence of two justices of the peace or one stipendiary magistrate; and a statutory declaration (*vide* below) must be made by two friends of the applicant before a commissioner for oaths.

FORM I.

REQUEST FOR RECEPTION INTO RETREAT

Under the Inebriates Acts, 1879 and 1888

To the Licensee of the Retreat

I, the undersigned, hereby request you to receive me as a patient into the Retreat, in accordance with the above-mentioned Acts, and I undertake to remain therein for calendar months at least, unless sooner duly discharged, and to conform to the regulations, for the time being, in force in the Retreat.

Applicant's signature……

The above named …… signed this application in our presence, and at the time of h so doing we satisfied ourselves that he was an inebriate within the meaning of the Inebriates Acts, 1879 and 1888, and stated to h the effect of this application, and of h reception into the Retreat, and he appeared perfectly to understand the same.

Dated this day of 189 , at

Magistrates' signatures { ……
……

Applicant's name in full……
Address……
Description……

Witness's name in full……
Address……
……

n this form in the presence of two Justices of the
strate.

FORM II.

STATUTORY DECLARATION

The Inebriates Acts, 1879 and 1888

We,……………………………………………………………………

……………………………………………………………………………

and ……………………………………………………………………

……………………………………………………………………………

severally, solemnly, and sincerely declare that

……………………………………………………………………………

who is an applicant for admission into the   Retreat, is an inebriate within the meaning of the Inebriates Acts, 1879 and 1888 ; and we severally make this declaration, conscientiously believing the same to be true, and by virtue of the provisions of the Statutory Declarations Act, 1835.

Signatures { ……………………………………………
{ ……………………………………………

Taken and declared by the above named,

……………………………………………………………………………

and……………………………………………………………………

at…………………………in the county of…………………………

this………………day of………………189…

before me……………………………………………………………

A Commissioner to administer Oaths in the Supreme
Court of Judicature in England.

To be signed by any two persons who are acquainted with the facts in the presence of a Justice of the Peace or of a solicitor who is a Commissioner to administer Oaths.

Patients under the Acts are obliged to remain for the period voluntarily fixed by themselves in the request for admission ; if they escape they can be brought back. To obtain alcohol renders the offenders liable to legal punishment. The rules of the Retreat forbid alcohol in any form, and ensure that the patient shall lead a regular life. The necessary forms can be had on application to the Retreat, the addresses of which can be obtained on inquiry.

H. D. R.

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H. D. R.

OPIUM POISONING, AND OTHER INTOXICATIONS

It is often said that the craving for stimulant and narcotic drugs is a vice of civilisation; the labour of righteousness and wisdom is too great a burden even to be borne—far too great to be contemplated. The most complacent of men has moods in which he wishes he were again a child; in which he regrets the momentary joys, the carelessness of things to come: once again he would "play around the den of sorrow." The "instinct of self-preservation" is something more than a clinging to bare life; it contains a desire for the fulness of it, for uncalculated pleasures, for happiness which comes without scheming, for release from the scheming which does not bring happiness after all: a man will lay down his life without a murmur, but if it is to be lived he would live it well.

It needs no long consideration to tell us that these despondencies and these regrets are no fruit of civilisation: the yearning for a deep draught of life is of all time; savage and civilised man alike are ready, if occasion serve, to drown care in fantasy, and through some magic arch of ivory to escape into the land of the blest.

With the advance of "civilisation" the use of such gramarye as lies in herbs is not more but less prevalent. Noah, as soon as the ark was well off his mind, was at least as ready as a city broker to seek a careless joy in wine. To bring higher kinds of excitement and variety into the lives of those who have laboured and striven, or lain in dulness and monotony, is the gift not of barbarism, but of the arts. When I used to hear that an educated man after half a lifetime spent in a Yorkshire dale had taken to the bottle, I was often disposed to sympathise with his yearning after the ideal; though his way of seeking it might not be all one could desire.

The iron rule of the tribal savage is compensated by times of corybantic excitement; and when a whole clan gets drunk at once there is no room for scandal; even when a whole village gets drunk there is no one, except a few wives who do not count, to condemn the festival: but if in the midst of a sober community we individually seek these fictitious consolations we find that scandal is awakened and moralists are alarmed. On the other hand, in times like our own no doubt the modes of indulgence are more refined and the occasions of it more secret. In the service a soldier given to drink is kept more or less straight by discipline and the lack of private opportunity; the same man on his discharge disgraces himself, the restraints upon him are less constant and severe. The more civilised, that is, the more various and interesting life becomes, the more, no doubt, will be the occasions of secret indulgence; but the temptation will be less, and, though we shall hear more of them, the sinners will be fewer.

Wherein lies the harm of stimulants and narcotics? If they are short cuts to happiness, why not use paths so pleasant? Do we not ourselves prescribe these things to men and women racked with pain, or worn out by labour and sorrow? That sometimes and for momentary purposes, or to those for whom all hope of life is void, we do administer them, is true; but we do it with the utmost precaution, knowing that they act by reducing life, not by enlarging it; and, moreover, that in their degrees they create an organic need which when satisfied brings no reward. Food to a hungry man fortifies his life; love to a lorn man enlarges it; sleep and joy refresh us for new adventures: but habitually to satisfy the craving for drugs like morphine and alcohol, brings nothing home but the continual dropping of their endless importunity. And this, as I have said, is because, in maiming life to diminish the capacity for pain, we likewise diminish the capacity for happiness also.

The highest functions, though they yield the most, fatigue us most; the machinery is at once the most complex, the most costly, and the least automatic. By the ardour of aspiration or the steadfastness of faith we strive to bring these functions into habits, and thus to build up pleasures to abide with us; yet in this exercise the frailty of man, civilised or barbarian, is revealed. Now it may not be true to say that opium and other such agents cannot do anything for the higher life; to some brilliant men the very treachery of them has lain in the fact that they have some mask of virtue. It is alleged of many such agents that their stage of oblivion is preceded by a stage of stimulation. How far this stage is but apparent, or how far it is real, is hard to say: a sedation of certain parts may throw other functions into an eminence which may be positive or may be relative. In persons of vivid sensations, to calm the commotion of conflicting impulses may be some enfranchisement even of the highest faculties. The stories of such lives as that of Coleridge suggest such a possibility; or even the effects of a quiet pipe upon smaller persons. In customary use of a particular sedative the system ceases to resent its presence, and thus the initial stage of real or apparent stimulation, which seems to play a part in the action of all narcotics, is less alloyed; though on the other hand the doses must be increased, and a time arrives when the drug does little or no more than satiate the craving for its own repetition. Again, after the time of excitement, and on the way to the stage of depression, a middle moment of grateful peace and irresponsibility is experienced: "Is there any peace in ever climbing up the climbing wave? Let what is broken so remain. The gods are hard to reconcile." This blissful period, however, as nervous degradation becomes established, is encroached upon by misery, as is the pause of the heart in disease.

Dr. Brunton finds that the narcotics of the alcoholic series have an affinity to the substances of which the nerve-centres are composed—that in all probability they enter into a loose combination with this tissue for a time and arrest its processes. Prof. Binz says "morphin, chloral, ether and chloroform possess a strong affinity for the substance of the cerebral cortex in man, which becomes thus unable to perform waking functions"; a saying perilously near the explanations of Dr. Diafoirus. Physiological chemistry is probably on the track of an explanation, but for the present we can formulate little or nothing of it. My own crude opinion is that narcotics have no element of primary stimulation in them; that from the first they arrest the function of the parts to which they attach themselves, the parts first invaded being the highest planes of nervous function. Thus released from control the functions of the lower systems take their play; and necessitous man, no longer "amazed among the thorns and dangers of the world," is reduced to the light and careless livery of the child. Gradually, however, the drug, tightening its hold on the higher, penetrates to the lower planes of structure, and so perverts even the grosser viscera of the body that gaiety ends in abasement.

Poisoning by opium falls readily into the two chapters of Acute poisoning and Chronic poisoning; in the former case the drug may or not be wilfully taken, in the latter wilfully always. Opium is never used, except in the case of infants, as a means of slow murder, for which purpose it is unsuitable.

ACUTE OPIUM POISONING.—Toxicologists are agreed that poisoning by opium may be regarded as poisoning by morphine. Dr. Stevenson says "the effects of the other active constituents of the drug are overshadowed by those of its chief alkaloid."

Although opium or morphine is used so rarely by poisoners, it is far otherwise in respect of another criminal purpose, namely, of suicide. Persons seriously suicidal often seem strangely indifferent to the amenities of the practice. So far from invoking a gentle angel of death, such persons, in their hatred of life, often seem to find a savage delight in rending the garment of the flesh violently from them. Moreover, temptation to suicide usually presents itself to the actor in a concrete form, as shooting, drowning, poisoning, and so forth : thus each suicidal person has his own fashion of seeking death. Still, among the less bloodthirsty suicides—in those who put an end to themselves, not in abhorrence of life, but in pique, fear of shame, or fantasy—opium, which offers a calm and painless death, is often the chosen means.

Again, opium is so commonly used as a medicine or as an indulgence, and, as a liniment or the like, is so often at hand, that accidental poisoning by its means is no rare mishap. Recent legislation, however, or modern intelligence which is more effectual, has lessened the number of these accidents.

The varying susceptibility of various persons to opium is remarkable. The extreme sensitiveness of children to the drug is well known; and, indeed, some adults fall into syncope on taking very small quantities—such quantities, for example, as may be contained in ordinary cough syrups. Two such cases have occurred in my experience—one in each sex, and both in persons otherwise of no eccentricity. Others again show a remarkable tolerance of opium, and, as in them the preliminary "stage of stimulation" is prolonged or is unblurred by malaise (as in the case of De Quincey and probably of Coleridge), they are the more liable to fall into habitual indulgence. A friend of my own, maddened by pain, took during one night pills after pills of opium, amounting, so far as we were able to compute, to some 18 grains in all. He slept very soundly to a late hour in the morning, rather to his comfort; and it was almost by accident that the enormity of the mistake was discovered. He had used some ordinary doses of opium in the previous week, but none in his life before. The minimum poisonous dose for a man cannot be defined, but 18 grains of opium would mortally disagree with most people.

It is said that on ingestion of overwhelming doses of opium features of excitement are absent, or nearly so. This statement must be taken with some discrimination. Cases are recorded by Tardieu and others, under the name of "*la forme foudroyante*," in which the patient falls almost at once into coma; the limbs are relaxed, and no response can be elicited from the skin or the conjunctiva. Death, in the coma which appeared at the outset, may occur within an hour, or even in half an hour. No delirium or convulsion is seen, and the final phenomenon, dilatation of the pupils, is seen almost or quite from the beginning. We shall make, of course, the obvious reflection that the characters of the symptoms may depend not merely on dose, or on personal idiosyncrasy, but on the conditions of absorption at the moment of ingestion.

In these fulminating cases symptoms of excitement may be imperceptible or altogether wanting; and this is more likely to be the case if a fatal dose of morphine be administered subcutaneously. But under ordinary circumstances, when the symptoms come on more gradually and may take half an hour or an hour to develop themselves, some signs of excitement of certain parts are not wanting. The skin is hot, the pulse is quick, the heart throbs or palpitates, the head may ache, or dreams merging into delirium may be witnessed for a passing interval. In this state, moreover, the pupils are minutely contracted. In some cases the agitation and hallucinations are terrific, and the reflexes vivid; such cases, I understand, are not very rare, but I have never myself witnessed such a one.

Stupor then gradually gains upon a period of excitement, which may be virtually absent, more or less transient, or more or less confined to certain regions or functional groups of the body. The face becomes more dusky, the blood-pressure falls (Binz), and the breathing is more slow and stertorous; no external irritation can awaken a response; the limbs are relaxed, the pulse feeble and irregular. The secretions, which, with the exception of the sweat, have been falling in quantity from the beginning, are now suppressed; the sphincters are relaxed, and the pupils dilate.

During the advance of this comatose state the patient is not only unconscious, but ere long he is not to be aroused by any noise or agitation; though for a little while such means may bring a returning flush to the cheek or a little more force into the respiration. Dr. Stevenson says that even after the face has become cyanosed or ashy, and the skin bathed in colliquative sweat, recovery may be achieved. If death occur, it comes by failure of the respiration: these acts become uneven, tidal, and even so slow as 10 in the minute. I have once or twice seen slight convulsive movements during the coma, but in the earlier stages of it. Some writers speak of intercurrent moments of awakening; at any rate false semblances of amendment are as common as they are deceitful.

The duration of the coma is rather variable, but never lasts more than a few hours; the duration depends, indeed, less on the quantity taken than on the temporary conditions of absorption and the tolerance of the individual. A persistent improvement in the depths of the respirations and in the colour of the skin would be the first sign of recovery; though, as I have said of false semblances of recovery, such signs must not be too readily accepted: moreover relapses are not uncommon, due probably to some renewed dispersion of the poison in the system. In acute cases in children Dr. Stevenson says that "the second stage of intoxication is often wanting, and severe collapse and complete unconsciousness rapidly supervene."

Diagnosis.—Although the candidate for a medical degree is often invited to give the points of diagnosis between acute poisoning by opium or by alcohol, and of these again from hæmorrhage into the pons Varolii, yet in some cases a positive diagnosis is out of reach; and in many more a diagnosis can be founded only upon such incidental circumstances as the smell of opium in the vomit or breath, or on such evidences of suicide as mental disorder, purchase of the drug, empty bottles, and so forth.

Unless the patient lie in the final stage, the pupils will be equal and closely contracted, and the unconsciousness profound. An alcoholic patient is rarely intoxicated beyond the points of struggling and swearing, under which emotions his pupils often vary in size. Albuminuria may result from the prolonged use of opium: on the other hand, evidence of the presence of morphia in the system of a comatose person does not exclude the presence of uræmia; it might even suggest it. From syncope the distinction should not be difficult, except in the last stage, when the state may partake of the syncopic character; yet even then the stupor and abolition of reflexes may direct the observer aright. General convulsions at the outset, if the outset were witnessed, would not suggest opium, but rather uræmia, or hæmorrhage on the surface of the brain; here again the almost invariable equality and pin-hole contraction of the pupils may assist us. Any unilateral symptom, indeed, whether paretic, spasmodic, or ocular, would divert the attention from opium; and a rise of temperature would direct our surmises towards cerebral hæmorrhage. In diabetic coma we may have the smell of the breath to help us; and the examination of a specimen of the urine, which may be drawn off by the catheter, will establish the diagnosis. Tidal breathing (Cheyne-Stokes) may occur in opium poisoning, chloral poisoning, cerebral hæmorrhage, diabetes, or uræmia. The state of the pupils usually suffices to distinguish opium from chloral poisoning, and from the latter their minute and equal contraction with sweating skin must, I presume, be distinctive.

Morbid Anatomy.—There is nothing in opium poisoning to distinguish the parts of the brain from these in other cases of cerebral "congestion"; nor is there any constant morbid feature of the lungs or heart. Osler, however, reports that extreme passive congestion of the bases of the lungs takes place, as in cerebral apoplexy. Medico-legal considerations do not come within the limits of this work.

Treatment.—The first indication, it is needless to say, is to empty the stomach: even if it be known that the poison was taken hypodermically this operation must not be omitted, as morphine in smaller or larger quantities finds its way into the stomach from the blood. To empty the stomach, the pump is the proper means. Emetics would probably act slowly or not at all: in the use of potent emetics there is a risk of smothering the spark of life. Yet if no pump be at hand, an emetic of mustard and water must be administered; or apomorphine may be given under the skin, but it is a very depressing agent, and in so profound an apathy the reaction to a drug, even subcutaneously introduced, may be slow and imperfect. There is also the theoretical objection to its use that apomorphine is said to circulate in the system as one of the derivatives of morphine, and one, moreover, to which some of the morbid symptoms are attributed. Besides emptying the stomach at half-hourly intervals, to remove the successive infiltrations of the poison which is said to enter its cavity, can we do anything more?

It is the custom, a custom in which I have loyally taken my part during many a weary hour, to "arouse" the patient by bullying him. He is cuffed, dragged up and down the room by relays of enthusiasts, pinched, singed ("brulures," Charcot and Bouchard, vol. ii. p. 633), flipped with wet towels, bawled at, and racked by electric currents strong enough to drive an omnibus. Now, although these measures do, no doubt, animate a medical student with his first real sense of doing some good in the world, yet, in my opinion, they are as useless as barbarous. I do not call them cruel (except "brulures," which may remain to fight another day), but they are to be dismissed with other mediæval instruments of torture as curiosities for the *Illustrated Short History of Medicine* of the twentieth century. What possible end can be served by flagellating a senseless corse? So long as the poison oppresses the nervous centres it is useless; when the poison is clearing away it is otiose. Of what possible service are shouts unheard, blows unfelt, salts and feathers unsavoured? It were as well to flash a lantern into the eye of a blind man to restore his sight. It is amazing to me to see these violent futilities still gravely prescribed by modern writers.

Two good purposes may possibly be credited to them: it may be alleged that such efforts raise arterial blood-pressure, and that the wet-towel business may stimulate the respiratory centre. Now we know little enough about the conditions which modify blood-pressure; that muscular exercise, or at any rate the first initiation of it, raises the pressure is true; but to this end there must be a function on the part of the patient: to haul a dummy about the room will only raise the blood-pressure of the attendants. If the respiratory function may be stimulated by "towel-ending," far be it from me by any gibes of mine to deprive the patient of such attentions. But seeing that we are in some measure independent of this drowsy nerve-centre, and can for a while perform the patient's respiration much better than he can, why resort to dubious means? Instead of all this rough-and-ready turbulence, relays of attendants should be deliberately organised for artificial respiration, and the respiration thus kept going in order that, as the poison is excreted, if happily it may be, the awakening centre may find that its work has been going on during its abeyance, and that its machinery is in working order. After clearing the stomach, artificial respiration and the inhalation of oxygen, and the application of warmth to the body and limbs, are the first and chief means of restoration. Now, can we do anything else? Are there any specifics which have the power of neutralising or counteracting the opium or the morphine? In the years 1864-65 Mr. Teale and myself carried out a not inconsiderable series of experiments upon this subject. We investigated especially the antidotal powers of atropine and caffeine, as these seemed then to us the most hopeful means. The experiments, however, we decided not to publish, for the reason that in the lower animals the degrees of tolerance vary within such wide limits that it was difficult to establish any standard. These irregular peculiarities of animals were then little known, and on account of them we wasted a great deal of time. I only refer to them now to record our strong impression that the antidotal effects of pure caffeine, obtained from Merck of Darmstadt, were not inconsiderable. Of atropine, Prof. Binz and Dr. Lauder Brunton say that it has an antagonistic action to opium up to a certain point, chiefly in its action on respiration—atropine acting as a stimulant, and morphine as a depressant on the respiratory centre. I have administered atropine in several cases of opium poisoning, and I have thought with occasional advantage, but certainly not with any great or consistent success.

In view of the depression of the respiratory centre it is well to inject small and cautiously repeated doses, watching the effects upon the function; but blindly to pour in a second virulent poison upon the first can never be pardonable so long as our knowledge on the subject remains as scanty as unfortunately it is at present. The obvious antagonism of the actions of these drugs upon the pupil may lead us to place too much confidence in the completeness of their opposition. Pure caffeine, however (not the citrate, which is not a constant drug), may be safely injected subcutaneously in doses of five grains; the dose may be repeated, and injections of hot infusion of coffee or green tea may be thrown into the rectum. The atropine may be postponed until the respiration falls; and then, as I have said, artificial respiration takes the chief remedial place. Cocaine is not to be thought of, as I shall explain under the head of "Chronic Poisoning." So far, then, our means seem to be evacuation of the stomach, injections of pure caffeine and of hot coffee, a cautious trial of $\frac{1}{50}$ to $\frac{1}{20}$ gr. of atropine, and artificial respiration, with perhaps the exhibition of oxygen, as the function becomes more shallow or uneven. The caffeine will also help the heart; and in my experience it is better to rely on this aid than to give alcohol so freely as is often recommended. It must be remembered that alcohol, although of use as a cardiac stimulant, is a narcotic poison, stupefying the brain. If some drug to invigorate the heart be required, strychnine subcutaneously administered would seem to be a better means.

Can we do anything more? In the United States Dr. Moor has aroused a great deal of interest by proclaiming the marvellous virtues of potassium permanganate in opium or morphine poisoning. Many other physicians have recorded successes with this antidote, some claiming priority in the discovery. It will be time enough to settle these claims when the value of it is established. It is alleged that this salt oxidises the alkaloid, and thus reduces it to a harmless state; and it must be admitted that by his observations, including a number of experiments on man (such as the administration of three to five grains of morphine followed by the permanganate), Dr. Moor has shown that the remedy has considerable power upon the poison while the latter is still in the stomach; it seems, indeed, whatever the other contents of the stomach, to have a special or selective action upon the alkaloid. It is clearly our duty, then, to inject a solution of the potassium salt (ten grains dissolved in six ounces of water) into the stomach at the time of using the stomach-pump; or, if the stomach-pump cannot be introduced, to administer it by the nasal tube. Although the introduction of the permanganate into the stomach, where indeed it may well lie unabsorbed, cannot directly neutralise morphia already absorbed, or administered subcutaneously, yet we must not forget that small quantities of morphine return to the cavity of the stomach, or find their way thither even if inserted subcutaneously (11). So far as this be true, the introduction of the permanganate is always a reasonable measure. Dr. Moor relates a case in which morphine was found in the stomach thirteen hours after 150 grains of opium had been swallowed. He directs us to administer half a gramme to a gramme of the antidote in an ounce of water every half-hour by the mouth; or as frequently to wash out the stomach with a weak solution of the permanganate. Whether its hypodermic administration be of any antidotal value or not, it seems at any rate to be harmless, except as a local irritant. In November 1895 Dr. Stanley Walker restored a man to life who had taken sixteen grains of morphine in solution, and was comatose. Fifteen grains of the permanganate were introduced into the stomach in three doses. No subcutaneous injection was made.

CHRONIC POISONING.—**In Children.**—Of the slow poisoning of infants and very young children by those narcotics which contain opium I have little or no experience. We are told that such practices may be suspected when an infant dwindles, turns sallow, and is constipated, or has diarrhœa with offensive stools. Incontinence of urine, if continence had been reached, may recur. With its sickly looks the patient loses appetite, and, when not under the influence of the sedative, is irritable and sleepless; hence of course the excuse for continuing the use of the drug. In children, as in adults, pruritus and albuminuria may be observed. It is said that not only are elixirs, and the like, containing laudanum or other opiates given to children, but even clysters also. The difficulty of treating such cases lies in the discovery of the cause of the ailment; on such discovery gradual withdrawal of the drug is all that is required. It must not be asserted, on the other hand, that opium ought never to be administered to infants: we have the authority of Dr. Eustace Smith and others for saying that opium may be of "extreme value" in their ailments. He tells us that no ill effects will ensue if care be taken to begin with a sufficiently small dose, and to postpone a second dose until the effects of the first have been ascertained. Thus, for a child of one year old suffering from purging, if one minim of laudanum have not produced drowsiness, another may be given in six hours; with these precautions the remedy will be well borne three times a day. Dr. West, if I remember right, advocated the like treatment; and in a timid way I have followed this practice for many years.

A curious assertion has been made by Dr. Happel, that the children of morphinists often show on birth the "symptoms of withdrawal" of the drug; that they readily become cyanotic, and need morphia and alcohol to rear them. Dr. Crothers, in the same discussion (34), added that these children not rarely become themselves morphinists or alcoholists in after-life. It must be difficult to distinguish between such a direct and specific influence and the more general forms of neurotic inheritance. Four cases recur to my own memory: in one case the child of a morphinist father was marked only by asthma, which probably was part of a neurotic inheritance independently of the morphinism; and the children of three morphinist mothers were fairly healthy. As the use of morphine diminishes sexual desire, the children of morphinist mothers are more commonly met with than of morphinist fathers. Such children are no doubt born in poison, and need most careful feeding and management to attain a fairly healthy state (Gossmann). Erlenmeyer saw a healthy child born of two inveterate morphinists; but on the other hand he reports that many such children are sickly, frail, and bloodless.

Chronic Poisoning in Adults. — (SYNONYMS: *Morphinism, morphiomania, morphiumsucht*).—We now enter upon the most important chapter of our subject, namely, of the opium-eater or morphinist. Chronic opium habits may be divided into three practices — that of the opium-eater, by whom the drug is swallowed in the crude state or in preparations of the crude drug, such, for example, as laudanum; the opium-smoker, who inhales sublimated products of it; and the morphinist, who injects a solution of morphine under the skin, or occasionally, it is said, into a vein.

It is neither possible nor necessary to enter into the whole matter of the use and abuse of opium by the opium-eater. The reader who has perused any great part of the evidence taken by the Opium Commission in India is aware that opium is used by a vast number of Her Majesty's subjects, and by thousands of others beyond her dominions, in the faith that the drug is useful to them, and is not abused in any ordinary sense of the term. Whether it be taken as an antidote to fever or other ill-health, or as one of those nervine agents which all people, civilised or uncivilised, discover—as we have discovered tea, coffee, and tobacco—to soothe the nervous system, to restore it after fatigue, or to endow it with powers of extraordinary endurance in lieu of rest or food, opium is used, rightly or wrongly, in many Oriental countries not as an idle or vicious indulgence, but as a reasonable aid in the work of life.

A gentleman, who consulted me frequently in his later life, took a grain of opium in a pill every morning and every evening of the last fifteen years of a long, laborious and distinguished career. A man of great force of character, concerned in affairs of weight and of national importance, and of stainless character, he persisted in this habit—which, indeed, I never was so presumptuous as to endeavour to suppress—as being one which gave him no conscious gratification or diversion, but which toned and strengthened him for his deliberations and engagements. He did not use tobacco, and the opium seemed to stand to him in the place of that aid. The habit had arisen on the proper advice of a physician who had found him liable to intermittent "gouty" glycosuria. The opium was continued, however, not on this account, but for its own sake. I name this case because it is the only one in which I have had occasion continuously to observe a moderate use of the drug in this country. In temperate non-malarious climates, however, opium is not required, or is better replaced by tea or tobacco. Opium is still largely used by dwellers on the levels of England which at one time were malarious; either because there is still in such districts some remnant of maleficence, or, more probably, from old custom. It may, however, be taken as a safe rule, in our own country at any rate, that the familiar use of opium in any form is to play with fire, and probably to catch fire. Of the moderate use of opium in other countries no final opinion can now be given; in adults of good character the physician must use his own discretion, but he must ascertain that the habitual daily allowance is not an increasing one. Any temptation to such an increase—say beyond two grains a day—should determine the habit at once. One who has given himself up to the use of opium may not uncommonly consume as much as half a pint of laudanum in twenty-four hours; and it is asserted that an Oriental may consume "several grammes" of opium in a day. Among Mohammedans opium is strangely supposed to have aphrodisiac virtues; they also use it as a surrogate for the forbidden alcohol, and, with more excuse, to help them over those terribly protracted fasts of which we in the West have no experience.

Opium-smoking, whether in Europe or elsewhere in the world, suffers condemnation not because of the direct mischief of it, which may or may not be great, but of the degrading circumstances of its pursuit; in Eastern towns it is the resource of the scum of the earth, and is associated with every kind of abomination. Apart from its brutish surroundings, the smoking, subtle and seductive as these fumes may seem to be, cannot in itself be so mischievous a practice as opium-eating or morphine injection. Throughout this article, for brevity's sake, I have assumed that the effects of opium and of morphine are virtually the same, as ordinarily they are; but the practice of opium-smoking seems to indicate some important differences. Morphine, if volatilised at all, is thus dissipated in very small quantity, and of the sublimate a great part must be collected about the pipe. None of the bitter taste of the alkaloid is perceived in the mouth of the smoker. The total amount of morphine in one charge is calculated to be no more than three milligrammes; now, even if twenty pipes are smoked in a day, which is, I am told, a liberal allowance, we have only a possible total of six centigrammes (about one grain) of morphia burned in a day; the chief part of this is literally burned and not sublimated at all, and of the rest more or less is deposited about the pipe. A modern lady morphinist would put the remnant under her skin six times a day, and call upon us to admire her moderation.

Again, it is found that the smoker does not prize those qualities of opium which contain the larger proportions of morphia, but prefers the Indian and Chinese drugs (principally that of Patna), which contain only 3 to 7 per cent of morphia. Nevertheless the ill effects of opium-smoking are too patent to be reasoned away; and the arguments of its innocence are sufficiently confuted by the existence and results of the practice. There is, no doubt, some quality in opium-smoke which enslaves the smoker; and Dr. Stevenson thinks that the intoxication is due to intermediate products—picoline and pyridine, and the like—which have marked physiological activities. This author, I find, is of opinion that the direct effects of opium-smoking have been greatly exaggerated.

Opium-smoking obtained a certain vogue in the United States, until it was ousted by the syringe; on the other hand, curiously enough, large quantities of morphia are sent to China itself as a "cure" for opium-smoking. The morphine is made up in powders, each of which contains about a third of a grain in some rice-powder; the powders are taken at lengthening intervals until the habit is broken.

The opium-smoker is not rarely a man of active habits; and in moderation, like other uses of such drugs, the practice may enable the user to do a great deal of work on little food. Indeed the testimony of many travellers seems to assure us of this. In such persons it may do no more harm than the inhaling of cigarettes. Mr. Morrison, in reference to travelling in China, says of one day's stage, more than twenty-three miles: "I was carried all the way by three chair-coolies in a heavy chair in steady rain that made the unpaved track as slippery as ice—and this over the dizzy heights of a mountain pathway of extraordinary irregularity. Never slipping, never making a mistake, the three coolies bore the chair with my thirteen stone, easily and without straining. From time to time they rested a minute or two to take a whiff of tobacco; they were always in good humour, and finished the day as strong and fresh as when they began it. Within an hour of their arrival, all these three men were lying on their sides in the room opposite to mine, with their opium pipes and little wooden vials of opium before them, all three engaged in rolling and heating in their opium-lamps treacly pellets of opium." Everywhere the author found opium-smoking, and nowhere could he detect any signs of physical deterioration in an exceptionally strong and hardy race.

In depraved persons and imbeciles, who will abandon themselves to anything, it gradually produces the opium cachexia—"the emaciation, leaden pallor, languor and utter neglect of person and duties of life," in which the influence of morphine seems to manifest itself. I am told that morphine injection also is by no means unknown in the modern East, indeed that it is driving the smoking out of the field; if so, the change may be an ill one. In competition with the smoking-shops, there are now shops where injections are to be had at so much the syringeful.

Morphine injection is by far the most important agent in the story of the consumption of this drug. The opium-eater was a portent, almost a bogie; the morphinist, with her syringe and case of tabloids, is a familiar object in our consulting-rooms, if not in any nearer relation. This terrible vice—a vice scarcely less than that of alcoholic drunkenness—is perhaps somewhat on the decline; partly because those who would draw to it are better aware of its evils, partly because medical men are better aware of the danger of putting the means of indulgence within the reach of a patient. The morphine syringe was invented during my student days, and I have been able therefore to watch the whole of its course in the world. I have read, indeed, since I began to write this article, that I was the first physician in England to point out the dangers of morphine injections, in a paper in the *Practitioner* for 1870; but Nusbaum drew attention to the danger as early as 1864. On the first discovery of the method the effects of small injected doses were seen to be so beneficial, so prompt in relief, so free from the stomach derangements of opium in its other forms, that physicians, little knowing what they were about, took readily to the syringe in whatsoever sort of patient, and actually, indeed, handed over the use of the instrument to nurses, even to the patients themselves: many persons were thus led by trusted advisers into temptation who would otherwise have been clear of it.

Nowadays whoso betakes himself to the morphine syringe does so of his own naughtiness; yet that there is a good deal of such naughtiness in this world may be inferred, not only from personal experience, a fallacious guide, but from the huge consumption of the drug. For instance, during the twenty-five years beginning in 1854 and ending in 1880, the quantity of opium imported into the United States increased from 72,000 lb. to 372,000 lb.; the population during that time, so far as I can gather from ordinary sources, no more than doubled itself. Now, in its medicinal uses the consumption would not show a very large relative increase; how then are we to account for so vast a relative increase? The question is a hard one to answer. There must surely be a considerable increase in its use outside the sphere of legitimate medicine; and we may suppose that the use of morphine as a self-indulgence accounts for a good deal. The proper medicinal uses do, no doubt, increase with the greater demand for skilled medical assistance which comes with greater wealth; yet the increase seems more than any legitimate demand can explain. That the drug is used largely as a means of self-indulgence cannot be doubted by any medical man of experience.

Now, who are the persons who thus indulge themselves? The prompt answer will be—the neurotics. Who, then, are the neurotics? Are we not all neurotics nowadays? In a later chapter of this work I propose to discuss the subject of neurasthenia as a whole, and this I must not anticipate. I will repeat, however, what I have said on former occasions, that quickness and sensibility, acute perception and alert muscular reaction, are not morbid characters, but the qualities of high breeding; these qualities, however, become morbid when they are developed in relative excess in the lower ranges of sensibility, the higher qualities remaining at their former mean, that is, relatively in defect. Now that which in higher centres we call control, and in the lower inhibition, consists in the reverse of this—in the cultivation of the higher planes of thought and sensibility, whereby the alertness of the lower is not diminished but transformed. Unfortunately, disease may reduce a man to the level of those who had never known a higher state, and a man of mobile and sensitive fibre may thus for a phase become a neurotic: such a one may also become a morphinist under the pressure of pain or other distress, but he is not to be spoken of as constitutionally a neurotic. Again, not a few elderly persons have been under my care for sciatica, post-herpetic and other neuralgias, and the like, for whom morphine injections had been used; from such sufferers, however, this means must be firmly withheld, for it brings them into this dilemma, that while the rupture of the habit is in later life a graver stress, yet its continuance, by the cachexia it produces, is in them more quickly injurious to health than in younger persons. The establishment of a morphine habit in old people too often means an inevitable bondage, and shortened and fretful days.

Another class of patients—not neurotic—presents itself to our consideration, namely, of those, young or old, who, smitten by incurable and painful disease, expect no long span of life. Do we rightly encourage in these the use of the morphine syringe? That in some such cases, as of aneurysm, for example, the practice may be the lesser of two evil courses, may well be; but the solace is purchased at a heavy price. Whether pain soothed by less treacherous means be better, not only for the patient's friends but also for himself, than tearfulness, petulance, caprice, and a deterioration of character, which makes the death-bed a scene of pettiness and exaction, rather than an example of fortitude and serenity, must be decided in the individual case. Too often a habitual resort to the drug, needed in increasing quantities, brings death of what is best in the man without euthanasia.

However, in some such instances the use of morphine may be the only alternative to pain, spasm or agony, otherwise not to be borne. Yet when we speak of pain not to be borne, we must not forget that there are two factors concerned, namely, the bearer and that which is borne. We have hitherto spoken of patients, not deficient in self-control, in whom this government is broken down by immeasurable pain. There are cases, far more in number, in which not the extravagance of the pain, but a weakness of will is concerned. In no case can we pretend to appreciate the pain of the patient, but we may form some opinion of his fortitude.

Not a few persons are led into morphinism by pain which is wearisome rather than acute. A remarkable instance of this kind of temptation was long under my observation. A business man of middle life, refined and intellectual but not to be called neurotic, who used his morphine syringe with unusual self-restraint, rarely perhaps beyond the measure of half a grain thrice daily, told his medical advisers that a wearing pain in the epigastrium deprived him of all pleasure, or even of capacity for life in business or society. In order to discuss an important matter with a customer he must inject morphine, or be unable to give his attention to the matter in hand. Not by myself only, but by other physicians, his abdomen was examined with negative results. We were tempted to suspect him of hypochondriasis; and, in spite of his economy in the practice, his life fell slowly to a lower plane. He got sallower, thinner, rather fretful, and at last, as is often the case in morphinists, he was suddenly overborne by an attack of acute disease of no great severity. A necropsy was obtained; we found a band of about an inch in length attached by one end to the walls of the abdomen, and by the other to the anterior wall of the stomach. This being in the very spot to which he had always referred the pain, we had little doubt that we had there discovered its cause. This band probably arose as a consequence of an ulcer of ancient date; but such draggings, whether due to slips, scars, or bands, may be the cause of morphinism in persons not more neurotic than the rest of us. A dragging of this kind may be at least as hard to bear as acute pain which usually presents periods of remission.

Again, a drag on the mind may act like a drag on the body. Sheer ennui, a luxurious life with nothing to feed the mind or fortify the temper, may lead to the vice. Want of exercise, over-eating, incessant and trivial social claims and emulations, with the disappointments, fatigue, or dyspepsia they produce, may be efficient causes of morphinism. Let a passing pain attack such a person, and therewith perhaps an unusual call on the energies, and to one thus driven and embarrassed an immediate relief suggests itself,—just this once, this one draught of brandy or ether, this one syringeful of morphine; there will be little interest to pay on so small an advance. These victims must be many.

Then comes the troop of those "neurotics"—persons subject, perhaps, by nature to larger oscillations of nervous balance than the normal man—who scent intoxicants from afar with a retriever-like instinct, and, curious in their sensations, play in and out with all kinds of them; narcotics possess such folk almost by anticipation, and they often find less difficulty in the first tolerance than other people. With conscience blunted, and the bit out of the mouth so that energy is set loose as it never was before; energy expanding under no self-criticism, energy joyfully soaring into extravagance with that bemused sense of brilliant ascendency which animates the "general paralytic" in his earlier phases—be it morphine, alcohol, chloral, cocaine, all or any are welcome: the intoxication with its hours of excitement and repose must be had at any price, and every reform is followed by a relapse into the use of the same drug or of another. It is in these persons that a hereditary craving for intoxicants is found; and with this tendency we may find in the family tree nervous disease or insanity; yet by no means always so. Individuals of such families, indeed, may naturally possess great intellectual powers, and may create splendid waking dreams out of drugs and wines which fuddle the rest of us—though it must be admitted that the records of these fantasies rarely bear out their report. It is curious to see how soon these persons become aware of their capacities, and even in their adolescence find their way to such potions as little ducks to the water, under however dry a hen they may have been reared. Gambling seems to break out in some persons in the same irrelevant way.

One more group of morphinists and I have done. I refer to those who take to morphine on small excuse, because it lies to their hand. Of these weak persons doctors and druggists form the majority; the rest are chemists and other men of science familiar with such means, who think in their folly that their technical knowledge will give them the use without the abuse of them. Unfortunately these very persons in their conceit become the most abandoned and the least reclaimable of them all.

In respect of sex there does not seem to be much difference; the anticipation that the practice would be found more prevalent in woman is not supported by facts. From my own experience I certainly should have said that the greater prevalence lay on the feminine side; however, Dr. Mattison, Dr. Levinstein, Dr. Erlenmeyer, and other authors of weight, find the figures to run pretty equally between the sexes.

The habit may be acquired at any age after the escape from tutelage into the temptations and cares of the world. When the practice is begun in advanced life, pain and medical or quasi-medical advice may give the cause and the opportunity. I have rarely or never known the morphine habit established under the weight of bereavement or other such heavy trial; alcohol or chloral seem to be preferred by those who cannot wait for the healing hand of time.

On the other hand, morphinism often arises from some discomfort or disorder following parturition. The syringe should never be used, not even in the hands of the physician himself, in cases of uterine disorder; slower but safer means of cure are to be found.

The total daily quantities of morphine which may be used by morphinists vary largely. In my own experience about fifteen grains seem often to have been the ordinary daily quantity, to be run up, if a servant give notice, or other real or imaginary worry occur, to thirty, or perhaps even to forty grains in the twenty-four hours. Other writers speak of quantities so large as sixty and seventy-five grains in twenty-four hours, the syringe being unscrewed from the needle as it lies under the skin that more of the solution may be injected on each occasion; on the other hand, some persons, none the less enslaved but with more self-control, keep the daily allowance down to two or three grains: morphinists who have relapsed after cure frequently manage to restrain themselves to smaller quantities, but too often by bringing in the supplementary aid of alcohol. Old persons, who in relief of some malady have fallen into the habit, seldom receive more than one or two grains a day, in repeated doses of a third to half a grain; but such persons are usually under some oversight and control. In making such estimates, however, we must not forget that the morphinist is so ready a liar that his assertions cannot be accepted without corroboration. My own largest figures are taken from the confessions of persons who have recovered, and not in all cases from my own patients, or from persons in any way responsible to me.

The symptoms of morphinism in the earlier stages of the habit are rather moral than physical. The stigmas of a morphinist are plausibility and disorderliness; and by these he may be known. Like certain other sinners who shall be nameless, the morphinist is ablaze with schemes for the benefit of his household, his parish, his country, and the world. He is usually a clever, and often an interesting person, sometimes even endowed with a rather "damaged" kind of genius; but owing to the perverseness of circumstances, nothing ever comes off.

So perverse are things, that if one did ever indulge a taste for drugs, the occasional aid—just for a week or two till things are straight—should be regarded as a venial matter, or indeed positively justifiable. If the patient come to the physician, he has had a dose within an hour; his pupils are contracted, he is voluble, ingenious in promises and excuses, and very tiresome. He is an hour late for his appointment, owing to the faults of others; if you call on him, you are kept waiting for as long a time as you choose to be detained. If he can avoid it, you do not see him in his ill-humours—querulous, exacting, slanderous, false, as he is in his domestic circle: yet the morphinist is never so lost as the alcoholist; his brain is not fuliginous; on the contrary, for some little time, the length of which depends on the economy of the drug, it is brisk enough. While the stage of elevation continues he is capable of doing a good spell of work in a spasmodic and irrelevant way; therefore, although slovenly, he is not chronically dirty, like a drunkard, but is capable once or twice a week of a good washing; and owing, perhaps, to an insensibility of the skin, his desire for "fresh air" is inordinate. A lady of this kind may come to a ball very smart indeed, though she will arrive when the rest of the world is departing. Her carriage was probably ordered for a drive at four o'clock, and she started at seven, astonishing some new friend by calling at an inconveniently late hour; she dined at 9.30, and arrived at the ball after midnight. In the morning to dress is impossible until the syringe has been used, and she is finally got to breakfast when the rest of the world is at luncheon. In the midst of all this ruin of time she stands complacent as the one faithful in a froward world. Meanwhile, no one can conceive how inconsiderately every one has acted to her, or wonder that occasionally, when thoroughly exhausted by her sufferings which are indescribable and her labours which are prodigious, she should use a very small dose of morphine. The only truth she tells (or he, I do not intend any preference of sex, but men are more under the compulsion of engagements) is that at odd moments she makes great efforts, efforts too often, though by no means always, ill-directed or futile. I have known many a morphinist who, if brought up to the scratch—and herein lies the difficulty—will acquit himself well as a public speaker, or even in more responsible duties if the exertion required be not continuous, or at a precise hour. This utter disregard of time is a marked feature of all users of narcotics, and of morphinists especially; so consistent are their inconsistencies of time and place, they almost succeed in throwing the revolutions of the sun into disorder. Dilatory they are, but even more are they diligent in contraries—*ὁμαλῶς ἀνώμαλοι*—turning night into day with a topsy-turviness worthy of Mr. Lewis Carrol.

The falseness of a morphinist cannot be glossed over as oblivion; though in part it may be that "Bemused in wine the bard his duns forgets, And drinks serene oblivion to his debts." The finer lines or, for that matter, the graver lines of ethical conduct become so blurred that the victims cease to regard them; thus their mouths are filled with lies, and if confronted with proofs of falseness the morphinist flippantly ignores them, or says he is driven to prevarication by the nagging or bullying of his friends. It is idle, of course, to argue with a patient with whom we have no common standard of veracity; and my own custom in all such cases is to say frankly at the outset, that, although I cast no aspersions upon the individual patient, it is my rule never to ask any question of a morphinist which requires a serious answer, or at any rate never to give any weight to the answer. I regret to say that this frankness arouses little or no resentment; such is the temporary "moral insanity" or moral anæsthesia established by the poison.

Thus far, then, the symptoms of morphinism are concerned rather with morals and conduct than with bodily disease. But if the habit be continued and the doses increased, as will be assuredly the case and that quickly, symptoms of bodily disease will appear; say in six or eight months at farthest. The flesh begins to fall; the face loses colour and takes on a sallow, lustreless hue and an aged expression; the teeth are loosened, and gradually even a young person becomes wizened, emaciated and haggard. To this rule there are some exceptions; I have seen a few patients who kept their flesh, or even grew fat and puffy: such persons are good feeders, take wine freely, and escape, I suppose, the catarrh of the stomach which attacks the greater number of their fellows. Constipation is always present, often in most obstinate degrees; the mouth is parched, and other secretions as a rule are arrested; though some morphinists sweat profusely. Still, for many years life itself seems to go on, and the constitution does not break up: morphinists do not, however, live to full age; and, if the habit be contracted in old age, the patient fades away in no long time. In younger subjects the social affections grow cold; waywardness and caprice deepen into selfishness and physical and moral degradation; the fitful charms of character or the powers of mind, if any such there were, are blotted and spent; memory especially fails; amenorrhœa and sterility overtake the woman, and impotence the man; irregular febrile attacks appear; albumin may be found in the urine; even sleep is heavy, or is exhausting and disturbed by hallucinations; abscesses arise at the punctures of the unclean needle, and heal badly; the mouth is dry; the teeth decay; gastric catarrh increases, with symptoms of nausea, retching and flatulence, and of an epigastric or substernal pain which is rather too characteristic of morphinism to be put down merely to the catarrh;[1] the thread of life grows frailer; all capacity even for fitful work disappears; the intercurrent miseries of the habit are intensified, the moments of excitement briefer and less effectual, until the patient curses the day he was born: in later middle life at farthest he dies, usually cut off quickly by some chance malady.

Pathological anatomy.—Autopsy is rare in cases of uncomplicated morphinism. The only important point herein is the state of the heart. Schweninger and others allege that fatty degeneration of the heart is to be found in these cases after death. I have no positive facts to guide me to an opinion on this matter; but on clinical grounds I have seen no reason to suspect its presence, either in the course of the malady or in a prevalent mode of death. To adduce, in proof of this assertion, cases in which other organic degenerations are found is to offer proof of too much or too little. The testimony of the best authors seems to be opposed to the belief that fatty heart is a direct consequence of morphinism. Wittkowsky's papers are helpful in this aspect of the matter. The observations of Binz on the fall of blood-pressure in acute poisoning of animals by morphine have little bearing on chronic poisoning. Bell says that chronic poisoning by morphine promotes hepatic steatosis.

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[1] Hitzig says that under morphine hydrochloric acid fails in the gastric juice, and that the cravings are due to returning acidity.

Diagnosis.—Chronic poisoning by chloral or the bromides may be difficult to distinguish from morphinism; but the diagnosis would rarely be of urgent importance. A difficulty may arise, however, in a case of delirium in a patient previously unknown to the physician. Morphine delirium may resemble delirium tremens or mania. Scars on the skin are to be looked for. The tremors in morphine delirium increase with the delirium, in alcoholic delirium they decrease. Morphine delirium may occur as well in women as in men; and the former may present hysterical features, such as contractures, screams or catalepsy. Albumin may be found in the urine in either delirium, but more frequently in the alcoholic form. The hallucinations in morphine delirium are less revolting, and its duration is rarely more than thirty-six hours. Finally, in this latter malady a morphine injection will probably give prompt relief. The history and character of the attack generally suffice to distinguish it from mania.

The diagnosis of a secret morphine habit is very difficult. Periods of excitement associated with contracted pupils have more than once led me to a correct conclusion; and the patient is pretty sure not to face the doctor without a dose. An excuse may be made to examine the arms, when scars may be found. Still this opportunity may fail and diagnosis be impossible without seclusion. Seclusion for twenty-four or thirty-six hours will certainly betray the craving.

Dr. Mattison has reported more than one case in which this habit was practised by a wife for years without the knowledge of the husband. That such instances can be cited is of medico-legal importance.

Prognosis.—If the habit be broken off, the constitution, even in severe cases, will appear to have undergone no profound deterioration; and the patient may regain all or much of his former health. The forecast in extreme cases must be estimated in accordance with the special characters of each. Authentic cases are on record of morphinists or opium-eaters, abandoned to the habit for twenty and even for thirty years, being cured completely by these methods, both in mind and body.

I have not found insanity to be a consequence of morphinism, save in persons in whom insanity was already potentially present. In persons with such a proclivity an access of insanity may be hastened by any reducing cause. Occasionally, however, insanity follows the use of morphia more directly; and if so, it usually takes the form of mania of persecution. The backbiting of friends, which is a common symptom in ordinary cases, becomes more extravagant and persistent. Except on withdrawal of the drug I have not seen the excitement or violence to which the name morphiomania would be properly applied.

In one or two cases of morphinism which have come under my notice the patient has died suddenly and unexpectedly; the presumption is no doubt that such deaths are due to heart failure. Relapses after apparent cure occur in about 70 per cent of all cases. To this danger I shall return.

Treatment.—There is one means of dealing with morphinism, and one only; namely, seclusion in a special retreat and submission to the discipline therein provided for such cases. Cures have occasionally been effected by home treatment; in the earlier years of my own practice, before special homes were in existence, I played a part in two or three such recoveries; but the enormous difficulties of curing the habit, if once it have hold of its victim, need no emphasis. A wife can have no control over her husband, nor contend against a stronger will clad in the armour of deceit; no husband has fortitude to turn a deaf ear to the terrible cravings and perhaps recrudescent neuralgias of his wife. No nurse, no medical man can keep up authority or carry out plans in such cases, without being overborne or deceived. A physician of mature age and experience cannot attend upon such patients without intermission; a young resident physician soon becomes powerless. Their wiliness is marvellous, and, under the most frank seeming, deception is surely at work: the physician may be certain that a tractable subject is getting the drug on the sly: unfortunately the latest and most careful chemical observers tell us that there is no trustworthy test by which small quantities of the excretion of morphine or of its derivatives can be detected in the urine.[1]

The physician is doing no kindness to the patient or his family if he trifle with the duty of insisting upon prompt seclusion. The patient himself will probably protest loudly; he dreads the horrors of the withdrawal, especially if he has been "cured" before; in spite of his better judgment he clings to his indulgence, and he harbours dreams of curing himself on the coming of that golden time when the trials of his world shall cease. Moreover, many such patients honestly think that the shock of withdrawal would be more than in their weakly state they are able to bear. To all these pleadings the judicious physician will lend no ear; he cannot, nor can any friend compel the patient to go into seclusion; but there are many material arguments which can be brought to bear upon a weakened will, not without success: moreover, the patient in nearly all cases is secretly desirous of escaping from his bondage—if it can be done without too terrible a wrench. If there be any local disease, such as uterine disease, renal or biliary calculus, as a source of pain, the utmost that can be done to relieve the condition must be done before the cure of the morphia habit is taken in hand; or the cure may fail under the pressure of recurrent pain. It is desirable to warn the friends of the sufferer beforehand that the period of detention, or at any rate of removal from home, may be as long as twelve months; but the time of probation can be better discussed when the means of cure and the tendencies to relapse have been considered. The first part of the cure is, of course, the withdrawal of the drug; and it is convenient, therefore, that I should now describe the

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[1] Dr. Hewlett has little confidence (I quote from a private letter) that by means of the "diazo-reaction" minute quantities of morphia (which could be detected in a colourless solution) could be detected in urine, especially in a high-coloured urine. Dr. Mattison, however, still relies on the iodic acid test, or "Bartley process": "To the suspected urine add carbonate of sodium to make it alkaline. In this put a portion of chloroform, shake well; allow to settle; draw off; and add a small amount of iodic acid. If morphine be present a violet tinge appears."

Symptoms of Withdrawal.—The chief and most grievous symptom is the dangerous collapse which may follow withdrawal, and if the withdrawal be sudden may reach an alarming and even a fatal degree. If the drug be wholly withdrawn at the beginning, an anxious restlessness and irresistible yawnings mark the approach of the time of craving; the knee-jerks, which were deficient or even absent, become exaggerated; anæsthesia gives way to hyperæsthesia; the patient begins to pace the room in a state of tremulous excitement, which becomes an agony; he springs sleepless from bed, he is shaken by rigors, sweat stands upon his skin, and saliva runs from his mouth. Feverless chills and creepinesses, or sharp accesses of pyrexia often simulating ague, sneezing fits, deathly pallor, sinking, nausea and hiccup are attended or followed by vomiting and diarrhœa; the pupils widen, and are sluggish in their accommodation; speech and even gait are as if palsied; hallucinations of vision, of hearing, and even of smell, take possession of the mind, and pass into a delirium often so violent that the cautious attendant will take care that razors and garters have been removed and the windows secured. At this stage collapse may set in, and at any moment; the physician, with his syringe charged with a small dose of morphine—say one-tenth of the accustomed dose—must not leave the patient's side for an instant. If the state become really alarming the dose must be inserted; meanwhile he will do well to keep his finger upon the patient's pulse, noting any irregularity or fall in pressure and rate; in this stage the pulse may fall as low in number as 40 or even 30 beats to the minute. Well do I remember such a night as this when I sat, syringe in hand, fearing death, but fearing morphine almost as much (for we had no means of isolation in those days), and after each attack of diarrhœa counting the pulse, touching the extremities, testing the consciousness, watching the laborious and uneven respirations, until with quickening function the need of morphine passed then and for ever from that unhappy life. The unemptied syringe was thrown behind the fire, and recovery from the degradation of years was accomplished. Twice from medical friends have I heard a like tale of cases within the sphere of my own observation. Collapse may come on unexpectedly even when diarrhœa has ceased; the patient becomes faint, the face pinched, and the voice hollow; the limbs may twitch; the pulse ceases at the wrist, and the signs of consciousness fail. This threatening condition may last even for an hour, or may be repeated again and again within the day. If the ordinary cordials fail to put off the danger the injection of a small quantity of morphine must be made, lest complete collapse set in. Fortunately this remedy never fails. Marmé is of opinion that the symptoms are due to poisoning by a derivative of morphine (oxydimorphine) in the system, the effects of which are neutralised by morphine. Clearly the collapse is no mere consequence of the vomiting and diarrhœa. As the sudden withdrawal of morphine is no longer practised this collapse may pass out of observation. Levinstein in Germany, and I myself in England, formerly advocated sudden and complete withdrawal; what Dr. Levinstein would now have advised we cannot tell; but for my own part I have become a convert to the plan of gradual withdrawal, and I believe Dr. Levinstein's practice was modified in his later years. I formerly opposed gradual withdrawal, because I had not seen a death in consequence of this sudden method (though I learn on good authority that such deaths have occurred), because I thought it more cruel to protract the misery, as it is more cruel to pull out a tooth slowly,[1] and chiefly because, in the absence of homes for isolation, it was important to get over the crisis before friends or patient should have time to interfere or repent. For the rupture of the habit once made the chain for the while is broken, and the danger of relapse is not so immediate as in the case of alcohol. Withdrawal once effected, temporary recovery at any rate is assured.

But if the patient can be consigned to a home where there is no danger of interference with the regular progress of treatment, I prefer a more gradual but yet expeditious method. A sudden withdrawal is not only more dangerous to the patient than a method which, though rapid enough to end the trial quickly, is not sudden; but also convalescence may be made more tedious by the heavier stress of the sudden method on the sufferer; and some symptom, such especially as diarrhœa, may persist and prevent complete recovery. If the prostration in the sudden method be so great that the patient is unconscious or semi-conscious, and knows or remembers little of his agonies, I admit, nevertheless, that the shock to the system may not be much less for the veiling of his consciousness, and the delirium may be so violent that for such cases a remote apartment should be provided in all cases. The advocates of the rapid (not sudden) methods allege, moreover, and I believe truly allege, that collapse never occurs except on sudden withdrawal. If this be so, it is needless to say that sudden withdrawal, save in mild cases, should be abandoned. Assuming, then, that we are not obliged to snatch our victory, and that the patient is secure in a kindly home, we should prefer the modified but still rapid method as practised by Dr. Mattison and other experienced physicians of these institutions.

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[1] A morphinist patient, experienced in cures and relapses, told Dr. Erlenmeyer that slow withdrawal is worse even than the sudden method. He compared the former to biting off a dog's tail bit by bit. All authors agree that withdrawal is more distressing to the injector than to the eater of the drug.

If the habitual quantity be small—by which I mean not more than three or four grains a day—the withdrawal in men may be sudden, and the matter thus settled off-hand. In women or shattered men a little more caution is necessary. Again, if the quantities be more than five grains a day, but the patient on the hither side of cachexia and emaciation, some briskness of reforming zeal may be justified, and the enemy expelled without much parleying. But in the case of those who have abandoned themselves to large doses, and are often cachectic, and brought low in nutrition and strength, the physician (and I need not say the physician only), after learning, so far as may be possible, the habitual doses and the customary hours of indulgence, may administer during the first twenty-four hours one-half of the usual quantity. Halving this again and again, in five to seven days the doses may reach the vanishing point. Although in some measure the usual hours of indulgence are to be observed, especially the last dose at night, yet the number of injections should be reduced as well as the total quantity of the drug.

It is needless to say that almost everything now depends upon the tact and integrity of the attendants, to whom enormous bribes may be offered. Nor must they fail in astuteness, for a morphinist is an astute person, and often has morphinistic or other perverted allies outside the house. The patient on admission must have a bath in order that all his clothes and person may be searched; he must be taken from the bath into a warm room, in which are none of his own effects; slippers, letters, books, and the like must be minutely examined, or not admitted. Allegations of sleeplessness must be accurately tested by the nurse's record.

By this method the accidents of collapse or violent diarrhœa are avoided on the one hand, and on the other we do not drag out the patient's sufferings unduly. Dr. Mattison in Brooklyn, while withdrawing the morphine as quickly as the individual state may justify, gives 30 grains of sodium bromide on the first day to ease off the suffering, and, adding 7½ grains daily, reaches 80 or 90 grains a day as the morphine comes to an end. He then gives 30 grains of trional every night for a week; reduces this in the week following to half the dose, and ends the case with a little chloral hydrate or paraldehyde. Other physicians inject codeine when all morphine is taken off; but it is not very efficacious, and injections should be got rid of as soon as possible, whatever the substance conveyed into the body.

Many other drugs are recommended by this physician or by that, as surrogates for morphine after the reduction or removal of the drug—such as chloralamide, sulphonal (said not to be so good as trional), monobromide of camphor, and so forth. For my part, as I have explained in the earlier part of this article, next to morphine itself, I find caffeine the most useful aid in combating syncope or collapse. For the same purpose copious hot-water clysters (105°) are useful and seem to soothe the diarrhœa. If the stomach be so disturbed that absorption is likely to be slow, then no doubt it is better to inject the caffeine. It is well also to throw hot, strong coffee into the rectum. The bromides, in my experience, are chiefly useful at the moments of excitement; but whether it be that I am hard-hearted, or that these periods are too evanescent to need special remedies, I am indisposed to give drugs which are of the nature of depressants. I am the first to admit that my experience is very small beside that of Dr. Mattison, yet I would deprecate the use of all or any of the narcotic substitutes, save in great difficulty; "ut succedanea sint alieni periculi." Give the hair of the dog so far as you must; graduate the descent of the doses of it to the vanishing point, and make the transition in the individual case as rapidly as the constitutional state and the grain of the habit will permit; but beware of teaching the patient the use of a new narcotic. Cocaine, which has been recommended as a temporary substitute, is a most mischievous agent, and is carefully avoided by all physicians who have experience in these conditions [see Section on "Cocaine Poisoning"].

Whatever the value of auxiliary drugs, the importance of nourishment is tenfold greater. Without the utmost care and urgency in feeding, the most promising cases may do ill. The dietary must be of the most generous kind, as the stress lies heavily upon the pined body. The gastric catarrh, perhaps always present in a greater or less degree, is a serious interference with this purpose. When the nausea and vomiting are troublesome, cold meat jellies, iced coffee with or without cream, iced champagne, and the like, must be tried by the mouth, and supplemented by nutritive enemas [see art. on "Dietetics of the Sick"]. As the stomach becomes more capable of work, turtle and other strong soups, and like generous and restorative foods, must be pressed upon the patient; and gentle massage used to promote absorption and blood formation [see art. on "Massage" in vol. i.] Alcoholic remedies must be used sparingly and omitted as soon as possible. As convalescence advances the nutrition very rapidly improves, massage may be more freely used, tonic douches carefully administered, and drives in the fresh air provided, which are better than bodily exercise; the massage produces as much muscular movement as the patient can bear without fatigue. It is said that cases of "hysterical neurosis," combined with morphinism, are often cured in the process of withdrawal which, indeed, in the latter parts of it, differs little from the method of Dr. Weir Mitchell. It is stated by several authors that on withdrawal of the morphia the sexual appetite, long in abeyance, may return vividly and even uncontrollably. It is therefore of the utmost importance that women should be attended by mature nurses of their own sex, and men by male attendants only.

It has been my misfortune to see the pains which led to the morphine habit return with the suppression of it; a most disheartening event. In one of these cases the patient was an old gentleman of seventy years of age; the other a lady not in a retreat, and not submitted to special feeding and massage. She remained emaciated, and, as her sufferings were renewed, her friends acquiesced in her return to morphine as the lesser evil of the two. The patient was not under full control, and the case occurred before Dr. Mitchell's method had attained its present beneficent vogue. During the last ten years we have all become more alive to the fact that in thin neurotics, whether submitted to formal seclusion and massage or not, the first duty of the physician is to press nutritious food upon the fastidious patient until a substantial addition to the bodily weight is regained. Physicians experienced in morphinism assure us, correctly I trust, that these recrudescent pains gradually disappear again if restorative treatment be persistently carried out.

After-treatment and Relapses.—I have spoken of seclusions, or at any rate of absence from home, so long as a year or a year and a half. How can this be necessary when the withdrawal is completed in a week or two, and the craving thus summarily overcome? In dealing with this part of the subject I have to speak first of the disposition to relapse; for it is upon this disposition that the insecurity of the results obtained by the above methods depends. On the whole, my own cases have shown no great tendency to relapse. Setting aside half-witted and semi-insane morphinists, and a few cases, treated in the past with less determination, in which returns of pain forced the sufferers again to summon the treacherous familiar to their service, the good results of the cases weaned under my observation or within my knowledge have been almost always permanent. In this respect my personal experience of morphinism has been far more satisfactory than of alcoholism; I have too often seen a reclaimed morphinist become more or less of a toper. Still I am bound to admit that published statistics do not bear out the permanence of the cures. In Germany the results seem to be less permanent than in England. Of 82 patients recorded by Levinstein, 61 fell back; 28 were women, of whom only 10 fell back—which speaks well for that sex; of 32 doctors, 26 fell back, an awful revelation of our frailty! Oppenheim also refers to the large proportion of backsliding doctors—male or female; in his figures 93 relapsed out of 250. Of 100 males in his series 42 were doctors; next to these came apothecaries, chemists, druggists, and others who by their calling are familiar with drugs, and in possession of them and of the means of their use. In a paper read at the meeting of the American Medical Association at San Francisco in 1894, Dr. Mattison reported that of 300 patients 118 were medical men; and in another set of figures 62 out of 125 were of our profession. We must admit, then, that of the backsliders our own profession furnishes a large proportion. So far as personal impressions may go without figures I find my own experience to point in the same direction; though I have seen several good cases of permanent cure in medical men: medical morphinists are not to be without hope. Dr. Osler's judgment is that the morphinist is "only too apt to relapse into the habit." My own impression is that if the alcoholics and wrecks of other sorts were separated from the heap, the record of permanent cures would stand far better than these figures indicate, figures which, properly of course, include morphinists of every kind and degree. In the case of a respectable sinner with good home, and friends to help him, I think a favourable prognosis may be given if after four or six weeks' residence in a retreat, according to the severity of the case, certain precautions, such as I will now set forth, be carefully carried out.

The After-cure. — All observers experienced in morphinism are agreed that, unless circumstances forbid it, the patient, after the withdrawal is established, say in two or three months, should take a sea voyage. Erlenmeyer well points out that of the many grave objections to a slow tapering off of the doses of morphine, not the least is the waste of valuable time which ought to be given to the after-cure. A personal medical attendant is not usually necessary if the health be restored; all well-found ships have a medical man on board, who must be made aware of the former habits of the patient, and be warned never on any pretext whatever to permit the patient the use of narcotics of any kind, or to administer them himself, except under some extraordinary circumstances. The voyage should last for some months. The travelling companion must be a person of some ascendency over the patient, whose will indeed is usually weakened by his previous excesses; and to him a grave warning against alcohol must also be given, for these dilapidated creatures, if they do not relapse into morphinism, often fall under the bondage of drink. If a sea voyage be out of the question some means must be found of establishing the patient's health while protecting him from that contact with the stress and harshness of the world which he cannot bear until nutrition is thoroughly restored. During this interval douches and other corroborants must be employed in order to steady the nervous system. But the cares and stress of the world are not the only stones of stumbling. M. Paul Sollier has described certain tides of recurrent craving which beset the convalescent; for twelve or eighteen months after the cure, M. Sollier says that crises may come on, lasting for twenty-four to thirty-six hours, during which time the patient is possessed by a sense of intolerable weariness, dyspepsia—shown by flushing after meals and loss of appetite—sluggishness, and even diarrhœa and "biliousness." That this is more or less true I can aver, though I have not so accurately observed these systemic fluctuations as M. Sollier has done. The times of trial presumably begin as overwhelming psychical yearning, and take their origin in the nervous system; the gastric and other symptoms being secondary to the nervous perturbations. However this may be, we know that such a recurrent strife may be the lot of the patient for a year or more after the weaning; and herein lie the reasons for advising a long tutelage, unless the patient can be carefully watched by his friends. If the patient have no judicious friends to secure him against these resurgent tides of temptation, a long residence under the discipline of an institution may well be necessary.

It has been held by the courts of the United States that addiction to morphia, even in great excess, is not sufficient alone to prove testamentary incapacity. I believe the question has not arisen in the English courts.

Hypnotic suggestion has been recommended as a cure for morphinism. I have no personal experience of the method, but I have taken some pain to discover its virtues. So far as I can judge, it is in mild cases only that this remedy has had even the appearance of success; and to send a patient quickly out into the world again under "suggestion" is to court the failure which will probably follow.

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On some other Intoxicants

Hasheesh poisoning.—The action of Indian hemp is upon the brain, it is both a deliriant and a soporific. In small or relatively small doses it gives rise to gay hallucinations, at any rate in some persons and races; it is also said to act as an aphrodisiac, the dreams being of a lustful kind. To Europeans, however, this description scarcely applies; the dreams are simply disagreeable. The drug produces in some persons a curious loss of sense of time and space (Lauder Brunton, Marshall); yet it is said that during the hallucinatory stage the patient may answer questions and even conduct himself rationally. The sensory nerves are benumbed and the pupil is dilated. There are no constant symptoms of respiration, pulse, or temperature.

It is stated by the "Indian Hemp Drug Commission" of 1893-94 that "its moderate use has no physical, mental, or moral ill-effects whatever." "Its excessive use injures the physical constitution, and may cause dysentery and bronchitis. It tends to weaken the mind, and may cause insanity sometimes. It induces mental depravity and poverty, but rarely crime. The injury caused by excessive use is confined almost exclusively to the consumer, and scarcely affects society." The Commission thought that careful inquiry reduced the proportion of real hemp drug cases. "Of 222 cases of insanity ascribed to hemp drugs in the Lunatic Asylum statements of 1892, only 98 are found on careful inquiry by the Commissioners to have any connection with them. The result is that of the whole number of cases admitted to lunatic asylums (in India) in that year only 7·3 per cent can be ascribed to hemp drugs, and if cases in which hemp drugs have been only one of several possible causes are omitted, the percentage falls to 4·5. . . . Hemp drugs cause insanity more rarely than has popularly been supposed, and the resultant insanity is usually of a temporary character and of shorter duration than that due to other causes." The latest account of hasheesh insanity we owe to Dr. Warnock, the able and energetic reformer of the Cairo Lunatic Asylum. I extract the following paragraphs from Dr. Clouston's review of Warnock's Report for 1895 in the *Journal of Mental Science*, October 1896:—

> Dr. Warnock has some interesting facts in regard to hasheesh and its mental effects. Of his 253 admissions in the *last* half of 1895, 40 were put down to the abuse of hasheesh, and 40 more to the combined effects of this drug and alcohol. Of 80 cases only 5 were women. In 41 per cent of all his male patients hasheesh, alone or combined with alcohol, caused the disease; while in only 7 per cent of his female patients was this the case. After stating that the habit of smoking Indian hemp is widely prevalent in Egypt, he asks: "Is there a form of insanity produced by this habit so frequently occurring or of so peculiar a type that it can be demonstrated by asylum statistics? And is hasheesh a potent factor in the production of insanity in Egypt?" His conclusions are: "1. I have no doubt that in quite a considerable number of cases here hasheesh is the chief, if not the only, cause of the mental disease. 2. I doubt very much if hasheesh insanity can be at present diagnosed by its clinical characters alone. Many hasheesh cases recover almost immediately on their admission, an abstinence from the drug being in such cases followed by a cessation of the morbid symptoms." This sudden and rapid recovery is the most pathognomonic symptom. He classifies the usual types of hasheesh insanity as being:—
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> "*a. Hasheesh Intoxication.*—An elated, reckless state, in which optical

hallucinations and delusions that devils possess the subject frequently exist. Sometimes the condition amounts to delirium, which is usually milder, more manageable, and less aggressive than that of alcohol, and exhibits none of the ataxic phenomena of the latter. Recovery takes place in a day or two, or less; and the patient usually recognises the cause of his excitement." In connection with this "intoxication" Dr. Warnock asks if the subject of it is to be held responsible for crimes committed in this state or not?

"*b. Acute Mania.*—In this type terrifying hallucinations, fear of neighbours, outrageous conduct, continual restlessness and talking, sleeplessness, exhaustion, marked incoherence and complete absorption in insane ideas are the prominent symptoms. Such cases last some months, and do not always recover.

"*c. Weak-mindedness*—with acute outbreaks after each hasheesh excess. These cases are very numerous. While in residence such patients are quiet usually, and well behaved, and only betray the impaired state of their brains by being over-talkative, easily pleased, lazy, anergic, excitable on small provocation, unconcerned about their future, and willing to stay in hospital all their lives. They show no interest in their relatives, and only ask for plenty of food and cigarettes. After being discharged such cases soon return in a condition of excitement—in fact in a mild form of type *b.* They then talk rapidly and rush about, pouring torrents of abuse on those near them; curse and rave on slight provocation; are sleepless, and for ever moving in an aimless way; are urgent to be released. They deny the use of hasheesh at one moment and boast of its wonderful effects the next. Besides these types there are numbers of cases of chronic mania, mania of persecution, and chronic dementia, alleged to be produced by hasheesh, but I have no means of verifying these allegations."

NOTE ON THE PHARMACOLOGICAL ACTION OF CANNABIS RESIN.—Dr. Marshall, assistant to the Downing Professor of Medicine at Cambridge, has made a few experiments on animals, and afterwards upon himself, with the resin cannabinol, isolated by Messrs. Easterfield and Wood of Cambridge. Dr. Marshall says (*Proc. Camb. Phil. Soc.* vol. ix. pt. iii. 1896):—

The effects produced were similar to those described by other observers as resulting from the crude drug, which are probably due to cannabinol. Messrs. Easterfield and Wood have shown that cannabinol exists in charas (the most potent of cannabis compounds) to the extent of 33 per cent, and that it can be obtained, in amounts varying with the activity, from all the cannabis preparations they have examined.

About 2.30 on the afternoon of 19th Feb. last, whilst engaged in putting up an apparatus for the distillation of zinc ethyl, I took 0·1 g.–0·15 g. of the pure substance from the end of a glass rod. The substance very gradually dissolved in my mouth, it possessed a peculiar pungent aromatic and slightly bitter taste, and seemed after some time to produce slight anæsthesia of the mucous membrane covering the tongue and fauces. I forgot all about it and went on with my work; but soon after the zinc ethyl had commenced to distil—about 3.15—I suddenly felt a peculiar dryness in the mouth, apparently due to an increased viscidity of the saliva. This was quickly followed by paræsthesia and weakness in the legs. Gradually my mental power diminished—I was no longer able to control the steps of the operation, and commenced to wander aimlessly about the room. I had the most irresistible tendency to laugh; everything seemed ridiculously funny. At times I felt more rational; but these lucid intervals gradually grew shorter, and I fell under the influence of the drug.

I was now in a condition of acute intoxication: my speech was slurring; my gait ataxic. I was free from all sense of care and worry, and consequently felt extremely happy. Fits of laughter occurred, especially at first, and sometimes the muscles of my face were drawn to an almost painful degree. The most peculiar effect was a complete loss of time relation: time seemed to have no existence. I was constantly taking out my watch, thinking that hours must have passed, whereas only a few minutes had elapsed. This I believe was due to a complete loss of memory for recent events. The occurrence of lucid intervals was also peculiar in many ways. They seemed to come on suddenly, sometimes, but not always, as if the result of an effort of the will; they lasted a variable time, being shortest when the symptoms of intoxication were most marked; and while in them I could converse in a rational manner and even direct the work of the laboratory to a certain extent. About 6 o'clock I had two cups of coffee, and afterwards feeling somewhat better walked home. The fresh air and exertion revived me. I ate a good dinner, afterwards read a little, and retired to bed at 11 o'clock without having experienced any symptoms of sleepiness.

During the action of the cannabinol my pulse rose from 60 to 96 per minute; sensibility as determined by pinching was blunted; and my appearance was described as "ashy pale." The pupils were somewhat dilated, but throughout reacted well to light and accommodation. At no time do I remember having had any hallucinations; no unpleasant after-affects were experienced, and the substance seems to possess no constipating action.

Smaller doses produced similar though less marked effects; with doses of less than 0·01 g. no distinct action was obtained.

In Dr. Marshall's case, then, it appears that the drug had a "happy" effect. In 1886, at Trinity College, Cambridge, three students, one of them an Indian, took some hasheesh in "Turkish delight"; the drug was apparently very unequally distributed, for this dose had no effect. A few days afterwards they consumed more of the stuff, and were poisoned. Mr. Wherry attended them. Some of them were sick, and lost their sense of time to such an extent that three weeks seemed to have passed during the time they were vomiting.

In one of the cases debility followed, and for some time (months) an extraordinary degree of appetite.

COCAINE and its salts have been largely used as a means of producing anæsthesia. They have also been recommended by physicians and others as a temporary substitute for morphia in the weaning of morphinists from their habit. The drug has, moreover, been used as a habit for its own sake—either the leaves are chewed, as by the native Peruvians and others, or the alkaloid is taken into the system, by injection or otherwise, in its pure state. Cocaine is derived from the Erythroxylon Coca. The use of it by the inhabitants of the Pacific side of South America goes back beyond historical times; and under the name of "Spadic," and other names, the leaves are largely used at the present day by the Peruvians and other tribes of Western South America. The leaves are chewed and mixed with lime, and, in the habits of those races, they seem to take the place that tea and the like do with us. Under the influence of the drug the Indian is said to perform rapid and long journeys, or to carry heavy loads on very small quantities of food. The abeyance of appetite is probably due to the benumbing effects of the drug on the coats of the stomach. Following the example of Sir Robert Christison, I carried some coca with me to the Alps on more than one occasion in the hope of humiliating my fellow-climbers by some feats of activity or endurance, but without success; the leaves were obtained from a trustworthy source, but they seemed on myself to have no effect whatever. I never rose above my common form, and I humiliated nobody.

The drug as taken by the Indians is said not only to endow the labourer with extraordinary powers, but also to have the cheering and exciting effects of a nervine stimulant. Among these people, however, it is said that those who use coca in excess fall into a marasmus. The Indians say that under the influence of coca they need no sleep; certainly insomnia is one of the symptoms of poisoning by the alkaloid.

I need not say that the vogue of the alkaloid is largely due to its uses by the surgeon. The virtues of this agent in producing local anæsthesia are well known. A 2 per cent solution of cocaine painted upon a mucous membrane, as on that of the eye or of the mouth, is frequently found a sufficient anæsthetic for superficial operations. By subcutaneous puncturings even a deeper anæsthesia may be produced; but the beneficent virtues of the agent in this direction are unfortunately rendered of less avail by its treachery in others. Cocaine is a rapid and often a deadly poison, and one which has its own incalculable ways with certain sensitive people. Some persons, who present no signs of the peculiarity, are very susceptible to the drug; children, on the other hand, show a remarkable toleration of cocaine, as of another mydriatic agent, atropine.

Acute Cocaine poisoning.—So far as I am aware, cocaine has never been used as a means of murder, though a few instances of suicide by the drug are recorded.

Far commoner are cases of mishap in the use of cocaine in surgery. In some of these cases of poisoning the agent was used in careless excess; in the large majority the drug was used in relative excess, no doubt, but without carelessness. It would be foreign to the purposes of this article were I to enter with any fulness into the management of cocaine as an anæsthetic; but after reading over many such records, I gather that the most dangerous use of cocaine is to inject it into cavities, whether natural cavities such as the bladder, the tunica vaginalis, and the like; or into abscesses or sinuses. Cocaine is also a dangerous drug to use in the case of broken-down or anæmic persons, especially of persons in whom there is reason to suspect degeneration of the vascular system. It is also better to avoid its use in highly vascular parts, such as the gums or conjunctiva (14). The general opinion of careful surgeons and experimenters is, that it is well not only to economise the dose, but also to dilute the solution of the drug to as low a point as 2 per cent. Dr. Hayes reports a case in which the use of a nasal spray in a 4 per cent solution caused delirium and cramps, and Dr. de Havilland Hall a case of poisoning by a nasal spray of 10 per cent. Dr. Mactier reports sharp but transient poisoning, in a man aged twenty-five, by four drops of a 5 per cent solution instilled into both conjunctival sacs. It is probably a good rule never to exceed 3 per cent in solutions for surgical use; yet children are said to tolerate solutions as strong as 20 to 40 per cent (Felizet). Still it can never be wise to presume upon such immunity; for Hayes records the case of a child in which death followed an injection of about half a grain into the urethra. Schede reports grave though not fatal poisoning, in a strong man aged twenty, by the injection of thirty minims of a 10 per cent solution into the urethra. Washing out of the urethra and bladder on the first appearance of the symptoms seemed to be of no service. As regards absolute quantities it is very difficult, as I have foreshadowed, to establish a limit of safety. So little as $\frac{1}{7}$th of a grain injected under the skin has been followed by slight symptoms, and half a grain not infrequently; though this quantity could safely be administered to most persons, and could not be very harmful to any. No doubt such doses disturb those persons only whose susceptibility is high; such persons are probably many, but there is no means of winnowing them out. Ordinary persons can tolerate a quarter of a grain well enough, and even a grain and a half. The reports of fatal doses vary from eight to twenty-three grains (15); Mr. Curgenven records a case in which ten grains were fatal to a woman. I once painted my own throat liberally with a 20 per cent solution of the hydrochlorate, some no doubt being swallowed. I cannot say how much of the solution, which contained one grain in all, was used; but I was conscious of slight hallucinations and delirium shortly afterwards, though the disorder was not noticed by those about me.

Not to pursue the pharmacological aspects of the subject, I will content myself with pointing out that cocaine is a very uncertain drug in its action; that the doses for individuals must be carefully approached in each case, and, finally, that solutions injected under the skin or into cavities must not exceed a 3 per cent dilution: indeed fifteen minims of a 1 per cent dilution is sufficient to use in a patient whose personal equation in this respect is not known, or in whose case the solution may penetrate raw surfaces or highly vascular areas, such as the gums. The minimum fatal dose is fixed rather doubtfully by McLane Hamilton at half a grain.

To paint upon unbroken surfaces much stronger dilutions may be used; indeed the drug is not readily absorbed by the skin, though it produces an anæsthetic action upon it. Mucous surfaces must be dealt with more cautiously. This anæsthesia seems to arise in all animals possessed of a nervous system — even in molluscs, crustaceans, and the like — when submitted to the action of coca. The action of the drug does not seem to be cumulative. Rules for the use of cocaine in surgery by Reclus (*Revue de Chirurgie*, 1888) seem to be regarded by those best able to judge as trustworthy and sufficient. Dr. de Havilland Hall says that the addition of half the quantity of resorcin to the cocaine solution diminishes the toxic and increases the anæsthetic effects: moreover, it prevents crystallising out and decomposition. Eucaine is now coming into use in place of cocaine as a local anæsthetic: it is said to be safer, and equally useful for that purpose.

Symptoms.—When a relatively excessive dose has been taken the patient becomes pale, faint, and giddy, and breaks into a sweat; he complains of creepings on the skin, palpitation, and a sense of anxiety in the precordial region; the pulse begins to rise rapidly in rate and to fail in strength, and he becomes loquacious, agitated, or even hysterical. The dilated pupils fail to react to light and accommodation; the respiration becomes panting; faintness passes into prostration with more or less loss of consciousness, and perhaps with convulsion; cyanosis deepens, and in grave cases Cheyne-Stokes breathing is said to occur. The muscular system suffers greatly: pains, often sudden and severe, are felt in the limbs, and cramps, unilateral or bilateral, take possession of them, chiefly on the side of the flexors, which may amount to general rigidity and even to well-marked tetanus. Trismus and tetanic seizures are also recorded (Schede). Some anæsthesia of the skin is to be determined from the outset if the patient be able to testify to it; but he may soon fall into a delirium with hallucinations, become violent, suicidal, or even homicidal (Bornemann); while on the failure of the sphincters urine and fæces are passed into the bed.

In cocaine poisoning, even in the midst of such grave symptoms as these, we may be more hopeful of recovery than in some other intoxications. The duration of the symptoms is short, whether they end in recovery or in death.

The treatment is such as the symptoms indicate: it consists in the horizontal position, the free use of alcohol and diffusible stimulants, such as ammonia, by the mouth, the rectum, and the subcutaneous tissue; the inhalation of oxygen, and, if necessary, artificial respiration. Intravenous injections of two or three ounces of normal saline solution are said to have proved helpful. Nitrite of amyl has been currently recommended as an antidote, but it can only be of use in case of those small doses which raise arterial blood-pressure. Large doses lower the blood-pressure. In case of recovery some nervous disturbance—such as insomnia, vertigo, mental depression, and tingling in the limbs — may continue for some days. If a fatal event ensue, the convulsions tonic and clonic, will continue and coma will set in, so that the status epilepticus is established. In some respects the symptoms may be likened to those of poisoning by atropine. If the drug had been taken by the mouth the stomach should be emptied.

Morbid anatomy.—The number of deaths from cocaine are few. It seems tolerably certain that the heart is found in diastole; and the nervous centres are said to be "congested." In this there is nothing very characteristic, and unless cocaine be detected in the organs of the body, the cause of death cannot be ascertained by autopsy alone. Ehrlich says that changes are to be found in the hepatic cells—a "vacuolary" degeneration: the cells are large and even enormous in size, the nuclei being atrophied. During life the drug is said to injure and destroy the leucocytes.

Chronic Poisoning. Cocainism.—Sensitive as many persons are to small doses of cocaine and its salts, yet by habit the doses may be enormously increased, as in the case of other like agents. Cocainists have frequently been known to take from thirty to forty grains in a day; but not with impunity: the effects of chronic intoxication by cocaine are even more terrible than those of morphinism. Like morphia and alcohol, and unlike coffee and tobacco, coca brings the consumer into hopeless bondage. I have never seen a case of cocainism in which this drug was sought from the beginning for its own sake; the two cases which have fallen under my notice were secondary to morphinism, a not uncommon sequence of things. It is alleged, however, that the habit is on the increase, that it is taken for its sustaining virtues in physical exercises, and again as a cordial in the "coca wine" so recklessly sold to the public. If there be cocaine in the wine the morals of the buyer suffer, if none those of the seller. Coca snuffs and lozenges are also sold for common use. The habit is said to prevail, chiefly in the form of hypodermic injection, in Paris and in the United States.

Symptoms.—The first effects of the drug, at any rate in those who are habituated to it, consist in a sense of well-being, briskness of perception, and removal of fatigue, which make the drug, like others of its kind, attractive to those who are at once keen for life and yet soon fatigued. Perennial joy and vivacity seem promised to them. The effect, however, is very fleeting, more fleeting than the gifts of morphine, and is bought even at a greater price. For these qualities the drug has been used in the treatment of melancholia; but the relief obtained is transient, and followed by a depression which more than undoes the momentary good.

So also with those who use cocaine for purposes of intoxication—depression and insomnia soon supervene, and the victim is drawn to the more and more frequent repetition of his doses, and to increase of the quantities of each. As this fatal bondage is tightened symptoms of chronic intoxication come on. The temporary prostration and nausea grow worse (that is, if the drug be withheld); the appetite fails; diarrhœa may set in; fits of semi-consciousness appear with no subsequent recollection of that which has passed; a persistent tremor invades the muscles, especially of the upper limbs, and the nights are sleepless. As the habit progresses more permanent signs of deterioration show themselves. The face becomes sallow, the eyes sunken, and the whole body emaciated; the will becomes weakened to the point of imbecility; the voice is enfeebled to whinings and fretful pulings; hallucinations possess the senses; the limbs become cold and tormented, as is the rest of the skin, with sensations as of creeping animals or vermin; the mind gives way, and delusions of persecution are prominent in the wreck of intelligence. If the habit be still continued the abasement becomes profound. I have read somewhere of a mother and daughter who had fallen into this abyss—a pair of gaunt, hollow-eyed spectres, whose demented functions moved only in the pitiless circle of self-intoxication—a ghastly automatism. Now few persons would fall into this pit were it not that the use of coca has been recommended, most unfortunately in my opinion, by some physicians as a means of escape from morphinism. Were the value of coca in this respect more than it is, so baneful a cure should have our aversion; but, as I shall show that it has very little value of this kind, and that indeed the end desired can be better attained in other ways, it is to be hoped that the cocaine habit will soon be forgotten.

It is said that the depression which follows the excitement of morphine is attended with a rise of arterial blood-pressure: the arteries tighten. If this be so, we can see how it is that the patient who, sinking under the loss of morphia, injects cocaine, finds at once a great relief. First in the epigastrium and thence throughout the system there arises a sense of warmth and comfort. Erlenmeyer, who observed the effect of 232 injections of cocaine in eight morphinists (five men and three women), and of four control injections in healthy persons, states that this, the first effect of the drug, is upon the blood-vessels. By the finger, which detects a widening of the radial artery and an increasing dicrotism, and by the sphygmograph, he found that cocaine, in large doses, acts in the first instance as a cause of vaso-motor paresis with arterial dilatation and falling blood-pressure. In small doses, Schede says, there is a momentary rise in arterial pressure. The effect of a large dose, which comes on in about five minutes, is, however, very transient, lasting not more than about twenty-five minutes. As the dilatation passes off the comfort goes with it, and the patient has to repeat the dose or to suffer the miseries of the withdrawal of two drugs instead of one only. Erlenmeyer gives a number of pulse tracings to prove his assertions; and, although I have no great trust in the sphygmograph as means of detecting variations of arterial pressure, yet these tracings seem to be of some relative value in supporting the author's conclusions both as to the character of the change and its transience. As the effects thus pass off a blunted appetite and a renewed insomnia intensify the patient's sufferings. Such a patient left to himself becomes enslaved to both drugs, and must run up the doses to large quantities—to 30 or 40 grains of each. As Erlenmeyer shrewdly says, the cocaine is far less effective in removing the morphine symptoms than is morphine itself; so that it is better to use morphine in the cure than this new and treacherous ally.

Prognosis.—The slavery of coca is worse than that of morphia; it is more destructive of mind and body, and harder to put aside. The morphinist still retains some desire to defeat his enemy, and is filled with gratitude, at any rate for the time, when the cure is complete. The cocainist, on the other hand, is so reduced in intelligence that he neither desires emancipation nor feels any thrill of joy when released; his brain is so bemused that he cares nothing for freedom. Hence the prognosis in cocainism is worse, even when skilfully handled in a retreat, than in morphinism; the course, if the mind is to be restored, must be much longer, five or six months at least, and the result is less definitely hopeful.

Treatment.—The only possible means of dealing with a cocainist is to place him in a retreat where such cases are treated with sympathy and skill. Chloral or trional are useful aids in combating the sleeplessness and distress; and massage and feeding in repairing the wasted tissues.

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ETHER.—The story of ether drinking is chiefly known to me in a pamphlet by Mr. Ernest Hart, which was republished by the author from the columns of the *British Medical Journal* of the 18th of October 1890.

A few cases of this vice fell under the author's notice, and thus he was led to make inquiries into the prevalence of the habit; he received replies from many correspondents, chiefly from medical practitioners and the clergy. We find from Mr. Hart's article that the veteran hygienist, Sir Benjamin Richardson, had long been aware of the practice; and that Mr. H. N. Draper had published an account of it in the *Medical Press and Circular* of the 30th of May 1877. Dr. Walter Bernard of Londonderry, whose personal experience extends over forty-two years, says that ether drinking has been known to him during all this period. Sir Benjamin Richardson says that this abuse of ether was introduced into Draperstown in 1846-47.

At Draperstown, in South Derry, the practice seems to have begun more than half a century ago, and thence the habit spread over certain parts of the county of Londonderry, and into the borders of Antrim and Tyrone. It is alleged that ether drinking is practised also in Lincolnshire, and Mr. Hart has reason to believe that it is by no means unknown in London. Two cases have come under his own observation, and many isolated cases have been casually reported. In one of Mr. Hart's London cases the habit led to death.

Enormous quantities of "methylated spirit" are consigned to Ireland by large manufacturers, and from this crude spirit the "methylated ether" is obtained by purification, and is sold in drams at the shops. Now while pure ether costs about 5s. a pound, the methylated ethers cost from 8d. to 1s. 4d. It is to the introduction of this cheap ether, and to the activity of the revenue officers in hunting down the illicit stills, that the prevalence of ether drinking may be traced. The story that the practice arose in an evasion of "the pledge" against alcohol in the time of Father Mathew, seems to be a "picturesque inaccuracy." Resident observers in Ireland trust that the practice, denounced as it has been, and not unsuccessfully, by the Roman priests, is on the decline. The large quantities delivered by wholesale houses does not lend much corroboration to this pious hope; for in 1889 the amount sold was only one-tenth less than in 1876. One large dealer stated to Mr. Hart that he sells about one ton a year of methylated ether in Ulster. Mr. Draper says that Omagh takes about 225 gallons yearly. One man at Cookstown lays in 50 gallons at a time from the purifiers.

The cheapness of the intoxicant seems to promote its use. Its retail price is about 1d. for two drachms, or even a ½d. for a drachm and a half. The Rector of Cookstown says that "in small poor grocery shops ether is sold without restriction, and it is hawked about in exchange for eggs and farm produce." One of the guards of the Derry Central Railway says that "the smell of ether in the third-class carriages on market-days is disgusting and abominable."

Mr. Draper tells us that the usual quantity of ether taken as a dram is from two to four drachms; and that this dose is repeated twice, thrice, or even four and six times daily. As it is almost insoluble in water, it is usual, except perhaps with the moderate drinkers, to take a mouthful of water first, and after the ether another mouthful of water. An experienced drinker by holding his nose can take a large quantity undiluted. There are tales of persons who would take so much as a pint during the period of an ether debauch. One draught—less than a wineglassful—will produce intoxication in any one unaccustomed to the drug.

The special temptation of ether, as compared with other intoxicants, lies in the transitoriness of the immediate effect; moreover, little or no punishment remains, such as nausea, dry mouth, headache, and the like.

Thus, what Dr. Norman Kerr calls "the drama of intoxication" can be repeated several times a day, and for a small outlay.

Even respectable people take the ether and without shame, pretending that it is useful as a medicine for "the wind in the stomach," and other ailments. It is largely drunk also at wakes and dances. Its effects are very rapidly produced, and the stage of excitement very marked. "Those under its influence shout, dance, laugh, and act like maniacs: if the dose has been heavy they may fall down writhing and foaming at the mouth. They generally recover soon, and feel low and depressed; and often then will renew the dose, for which they have a strong craving." "A smaller dose is exhilarating, and produces a feeling of lightness as if the person could fly."

Profuse salivation often follows the drinking of ether, then rather violent eructations; the face becomes flushed, and, if large quantities are taken, may become livid: afterwards pallor, weakness, and burning pain at the epigastrium are felt. When the dose is large, frenzy, maniacal excitement, and ultimately stupor supervene.

Dr. J. W. Watson (quoted by Hart) says: "The ether drinkers agree that it is a very pleasurable form of intoxication, and others can see that it is a very violent form. But the most violent form is produced when whisky and ether are both taken."

Ether drinkers are very quarrelsome in their cups, the intoxication being decidedly of the pugnacious kind.

Pathology.—Of the remote effects of ether little is known. Sir Benjamin Richardson almost regrets that no grievous lesions arise in these subjects to point the moral of excess as in alcoholic drunkards. Chronic gastritis and dyspepsia seem to be the chief consequences. Ether drinkers, however, suffer from debility, great nervous prostration, tremors (especially in the neck and forearm), indigestion, irregular action of the heart, subacute gastritis, a peculiar whitish sallow complexion, and, in some cases, a peculiar livid cyanotic face. Dr. Walter Bernard (quoted by Hart) says that there follow wasting both of fat and muscle, enfeebled circulation, pale lemon or brown skin, exaggerated reflexes, and profound degeneration of the moral character. The victims fall into a kind of hysterical state, lose all self-respect, and will lie and steal to procure their favourite stimulant.

There does not seem to be any evidence to prove that ether drinking directly produces insanity; though of course it may favour its occurrence in persons thus disposed.

The habit leads to crime only through the violence and pugnacity so characteristic of this form of intoxication. In discussing the physical consequences, we must remember that these have not yet been thoroughly investigated by pathologists armed with the resources of modern science.

It is stated that the Government official restrictions imposed upon the sale of ether, as the result of Hart's reports on this subject, have greatly reduced the vice in Londonderry and Tyrone.

Chloroform, Chloral, Sulphonal, etc.—It is not necessary to enter into details concerning each one of these and other hypnotics or analgesics. They all bring about a loosening of the framework of the higher nervous matter, and thus weaken the will and the intelligence, and slacken the control of the emotions. Judgment becomes uncertain, action capricious, and temper fretful. The muscular system also, in its enfeeblement, weariness, and tremor, shows a like undoing. As with the former agents, here too there is a craving for the habitual drug: without it insomnia distracts the sufferer. It is often wise for a time to use another drug of soporific virtue in place of the old one, in order to shunt the morbid process before arresting it suddenly. But all bad cases of the kind should be treated in some retreat, whether it be the house of a medical man of skill and shrewdness, or a special institution.

An old and wholly sane friend of mine, who too often took sulphonal to counteract senile insomnia, astonished a number of his friends one morning by telling us with great particularity and gravity that, as no doubt we were aware, there were little red butterflies in the streets, which settled on the pavement or flitted in the air as they were disturbed by the stick or footstep of the passer-by. He seemed surprised that we had seen nothing of the kind, but no doubt of the reality of his own experience came into his head.

It is asserted that sulphonal destroys the red corpuscles of the blood, and, clinically speaking, patients whom I have known to be eaters of the drug wore an anæmic aspect. It is, moreover, asserted that its use produces a mild dementia. Calmness may be obtained at the expense of lucidity.

The habit of chloroform inhalation is especially to be dreaded; fatal accidents are not unlikely to occur in its use by the patient, as the annals of too many households can testify. Chloroform readily relieves asthma and other spasmodic affections; and if the medical attendant cannot prevent the use of this drug he must insist that it shall never be self-administered.

Chloral and chloroform differ in this important respect from other narcotics, that no full tolerance of them is established by habit. However persistent the habit may have been, even a moderate dose may suddenly prove fatal. The physician cannot too strongly impress this treacherous property of the drugs upon any patient who resorts to their use.

If taken internally in large quantities with suicidal intent, chloroform is an irritant poison, and the stomach-pump must be used carefully. Marfan (*Mercredi med.* No. 50, 1892) speaks of such a case in a man of fifty years of age who had swallowed 60 grammes; the internal pain was intense, and was followed by hæmatemesis and sanguineous slimy diarrhœa. The sleep lasted twelve and a half hours. On the following day jaundice set in, with enormous swelling of the liver and, in much less degree, of the spleen. For three days there was anuria; then urine appeared scantily, and was loaded with albumin and tinged with bile. There was occasional epistaxis. The urine became normal in fourteen days, when the jaundice and liver swelling had also subsided.

A case of chloral poisoning was recorded by the late Mr. Hulke in the *Lancet* of November 3, 1894. Five drachms of chloral were swallowed, but recovery followed. The means used were artificial respiration, and hot coffee administered freely by the bowel and otherwise. In such cases I think that the inhalation of oxygen should be tried. I have read that, if the coma be fatal, hyperpyrexia may ultimately appear. The subcutaneous injection of strychnine need not be omitted, but it is not obviously useful.

In the *Lancet* of July 20, 1895, Dr. Wright Hardwicke records the case of a dipsomaniac woman, aged thirty-seven, who, after consuming a variety of strong alcoholic drinks, including turpentine, chewed up some sulphonal tabloids to the amount of 265 grains. She was found shortly afterwards in a state of stupor. Five hours later she was seen by Dr. Hardwicke, who found her sleeping on her side with her knees drawn up, and the pupils slightly contracted and insensible to light. When roused she smiled graciously, and lapsed off to sleep again; she tried once to raise herself in bed, when she fell powerlessly back again. Next day the legs were found to be extended, and the soles of the feet were arched in a state of extreme flexion. The bowels were confined. She slept from 5 P.M. on June 1 till 5 A.M. on the 4th—sixty hours; she did not regain speech till the 7th, nor the power of locomotion till the 9th.

TOBACCO.—The effects of tobacco, for better or for worse, are so well known that it is not necessary to delay the reader by a long description of them.

Acute poisoning by tobacco can only occur by so strange a mischance that this part of the subject certainly need not be dealt with at large. If tobacco were swallowed in poisonous dose, the stomach-pump must of course be used, and tannin may be administered to neutralise the nicotine. The resulting symptoms must be treated by stimulants, such as subcutaneous injections of ether and the like. The enema of tobacco, once employed in medicine, was apt to be followed by dangerous consequences, and has properly fallen into disuse.

Chronic tobacco poisoning, now that snuff-taking has practically ceased, is met with in smokers only. How prevalent the smoking of tobacco has become in this century I need not say; but, so far as my personal impression goes, the habit seems to be a little on the decline. Among the undergraduates of Cambridge I certainly think the habit is not quite so general or the consumption so large. How great a consumption of the drug we are to call excessive it is impossible to say. That tobacco used moderately is generally injurious seems improbable, at any rate the mischief of it is not proved. The consumption of the drug, even in considerable quantities, as he who runs may see, is in many persons compatible with excellent health and with the propagation of sound progeny. Observers who assert the contrary point to town-bred youths, in whom other mischievous factors are at work.

In training, however, I am sure that the use of tobacco, like that of alcohol, should be much reduced, and for the most part postponed until the end of the day's work. The Alpine climber who nips at alcohol during his work has the odds against him; he becomes a second-class performer. The same is true of the use of tobacco; the disadvantage is much less, but the wise man will be content with one pipe on his peak when the main part of the day's work is over, and will keep the moderate rest of his smoke for evening. Thus used, tobacco is not injurious to most persons, and may have its indirect benefits in soothing fatigue and restlessness. It is, however, as true of tobacco as of other agents affecting the nervous system, that the personal equation is to be regarded. The quantity consumed with impunity by one man is poisonous to another; each smoker must estimate his own resistance and regulate his doses accordingly. Vertiginous sensations, tremor, treachery of memory or of utterance, cardiac flutterings, insomnia, should be at once regarded as warnings. If a smoker who is not quite a novice become aware of such symptoms he may be assured that he is not endowed with much tolerance, and must smoke with caution. Perhaps all persons by persistent effort can establish some measure of tolerance; but the susceptible person remains relatively obnoxious to the drug, and is more likely to suffer from evil consequences than others more hardily constituted in this respect. There seems to be no means of detecting liability to tobacco intolerance beforehand; many persons of instable nervous system may be less able to withstand such influences, but, on the other hand, many persons of strong nerves are very sensitive to tobacco. Although for medical reasons I have advised some few women to smoke on the sly, yet I have no hesitation in saying that the nervous system of women, being less under control, is more easily affected by such practices than that of man.

It has been asserted that cardiac irregularity and other symptoms of abuse of tobacco only occur in persons who smoke Havana cigars. That Havana cigars are more actively mischievous I have seen in my own practice, but pipes and cigarettes are likewise efficient, if in less degree.

To the unaccustomed person the poisonous properties of tobacco are sufficiently manifest. "Every schoolboy knows" the deadly pallor, the cold sweat, the horrible nausea, and, if he go farther, the diarrhœa and collapse which follow the first doses of the drug. That he should persist in a discipline so repulsive is an example of the scarcely voluntary functions of man in that imitative stage which is seen in the individual as it is in the uncivilised nation or tribe—the stage which lies between automatism and the free play of reason.

No less strange is it that tolerance is so readily established; individuals, however, vary widely in this readiness, and, as I have said, a young man who finds some difficulty in this part of his education will do well to regard himself in after-life as one by whom tobacco should be used with economy.

In the next place, we have to consider the ill effects of tobacco in those in whom the use has become habitual.

Among the slighter consequences are decay of the teeth, which few smokers escape; chronic granular pharyngitis, if this imposing name may be so applied; and muscular tremor. In respect of severer consequences there is still some difference of opinion: most people are agreed that with one exception, namely, atrophy of the optic nerve, the degenerative diseases of the central nervous system—such as tabes and the like—formerly attributed to tobacco were but coincidences. Tobacco amaurosis seems to stand alone among mischiefs so grave; and for a further description of this affection the reader will consult an article on medical ophthalmology which will appear in a later volume of this *System*. Whether epithelioma of the lip be a direct consequence of tobacco smoking is an open question; so many persons smoke regularly that it is difficult to apply the method of concomitant variations in this case. It is probable that in a person so disposed, the careless use of a short or hot pipe may favour the manifestation of this evil. In a person not so disposed it seems improbable that the evil would thus be induced.

Of lesser ills vertigo is not a very uncommon sign of excess or of intolerance of tobacco. It may be so severe as to disable the sufferer, or even, as in one case of my own, to throw him into bed. This symptom I have noticed rather in those who smoke cigarettes, perhaps because in this practice the smoke is generally inhaled. It must not be forgotten also that cigarette smokers get through a great deal of tobacco; twenty cigarettes a day is a common allowance, and fifty by no means an unknown one. But the symptoms may appear on the use of a pipe or cigar. While speaking of vertigo I may conveniently say that the effect of an habitual drug, be it tea, tobacco, alcohol, morphine, or other poison, cannot be thoroughly tested under six weeks' abstinence: if a patient will not give his word to observe this interval it is better to decline to advise him. A reduction of the allowance is of no use; it only leads to bewilderment both of patient and doctor: time must be given for the elimination of the poison, and, thereafter, for the tissues concerned to recover themselves. When, after the due period of abstinence, a judgment has been formed, and moderation has been accurately defined, the habit may perhaps be resumed.

After vertigo symptoms referable to the stomach and heart are most frequently found. A grinding pain of a peculiarly disquieting kind may come on fifteen to thirty minutes after food: this pain I believe to be due to hyperacidity. If so, the effect is the converse of that of morphine [see article on "Morphine"]. The pain is relieved by alkalies, and also by taking food again, as in the dyspepsia of hyperchlorhydria. Flatulence of the stomach is often met with in smokers, but usually in connection with irregularity of the heart: this flatulence is often met with in other affections of the heart, and it is hard to apportion the causative relation between the two events. Cardiac irregularity is a frequent consequence of tobacco smoking, lagging and intermission being the earlier forms of it. One case is known to me of a man whose general health is excellent, who is by no means a neurotic subject, and whose heart stands work well in all other respects, in whom intermittence of the heart may occur for many days if he remain for an hour or two in a room with many smokers. He dare not sit in the smoking room of his club or in the smoking compartment of a railway carriage. The intermittence may not begin until the next day, or the next but one, but then comes on with the certainty of a laboratory experiment; it gets worse during the next day or two, and then gradually passes off in a few more days. He never suffers from any cardiac disorder unless exposed to tobacco, but this proclivity has hung about him for many years. He has no dislike to the drug, nor does he feel any immediate discomfort from it. In actual smokers, even in those who smoke not immoderately, this proclivity is common enough. I remember finding the symptom in two brothers of about thirty years of age who came to me for life assurance. They were both fine vigorous men of good family stock, and they were naturally much nettled by my declining them. After leaving off tobacco for four or five weeks the intermittence disappeared, but as they both declined with some asperity to give up the habit I felt it my duty to decline them again. I am well aware that tobacco is said to affect the nerves of the heart only, and not its muscle; but a long experience of such "functional derangements" in this vital organ has led me to the opinion that ultimately such hearts come to no good. Cardiac irregularity under the influence of tobacco is not confined to intermittence; it may go on to utter disorder both in rate and rhythm (delirium cordis). The usual form is for two or three strong or throbbing pulses to be followed by a run of small quick ones; the blood-pressure being low in all. Occasionally in intermittency the stops may have a regular distribution, as, for instance, at every third or fifth interval. One day on seeing a friend of mine take again and again from his case a long and malignant-looking cigar, I remarked that such indulgence must disturb the action of his heart: his only reply was to hold out his wrist to me in order that I might touch one of the most irregular pulses I ever felt. He told me that tobacco had this very effect on him, but that he had long made up his mind that he would rather have his cigar than a model pulse. "Tobacco hearts" are common enough in young men who smoke freely before becoming thoroughly seasoned. The main feature in these youths is palpitation; and I think that any one who is experienced in these patients can detect a tobacco heart by the ways of it: it has a laboured and hesitating gait, different from the ordinary "young man's heart" and from the effects of organic disease. The hesitation is usually accompanied by a sense of discomfort referred by the patient to the cardiac region, to his heart. In tobacco intermittence the patient is, I believe, always conscious of the stop and roll forward, a sensation which in disease of the muscular tissue of the organ is not always but generally absent. The discomfort in the cardiac region is the first symptom to be noticed.

So far as I am aware, no careful autopsy has yet been made in a case of tobacco heart.

Insomnia is said to be a consequence of smoking tobacco under certain circumstances. Every smoker knows that a stronger cigar than usual may keep him awake; and it is alleged that the ordinary use of the drug may act thus as an excitant in one whose brain is unusually susceptible, or is in a state of irritability from overwork or anxiety. Usually the effects of tobacco are soothing and favour sleep; yet, like other narcotics, tobacco has no doubt its effects of stimulation.

The last group of symptoms of chronic poisoning by tobacco which I shall discuss is the group of neuralgias. These are of some importance, as until the cause is removed the pain may be recurrent and severe, and sometimes the cause is not hit upon. In one smoker I remember that the neuralgia was seated in the anterior crural nerve and was acutely lancinating. I forget what led me to suspect the patient's tobacco, but happily the suspicion was awakened; in abstinence he found perfect relief, and, as a return to tobacco was repeatedly found to recall the pain, he determined to remain abstinent and well. In other cases, and much more commonly, the pain is about the intercostals, and the humeral and scapular regions. Dr. Judson Bury records peripheral neuritis as a rare consequence of the use of tobacco.

A violent and alarming form of this pain is the so-called tobacco angina, described by Peter. There is not much difficulty in distinguishing tobacco angina from the form which depends upon cardio-vascular disease; but the diagnosis is not to be made by the mildness of the pain. The most frightful attack of tobacco angina (if so it is to be called) that I ever saw was in a gentleman then no longer young (about 55 or 60), who informed me that he often smoked as many as twenty cigars a day. He exhibited a specimen to me lest I should be under any apprehension that his cigars were small or mild. While actually in consultation with me he fell into a fit of the "angina," which was so severe as to make him writhe off his seat and, over the edge of a couch, to the floor. He pressed his hand to his heart, groaning piteously, if that could be piteous which witnessed in his favour. No man in an attack of true angina writhes or groans aloud; nor does a true attack last long enough for manœuvres of this kind. The note of angina pectoris is terror-stricken stillness; the patient dare not even breathe, lest he die in the act. Moreover, except in the rare "chronic" form of angina pectoris, the attack does not last so long as in the tobacco form; and in chronic angina there is rather a persistent series of attacks than one attack of long duration. Yet the tobacco seizure likewise may sometimes be startling in its suddenness, and in its likeness to angina pectoris. I remember hearing with anxiety the story of a healthy man, about fifty years of age, who in pressing hastily and with some anxiety up a steep hill in a fog, was seized in a moment by a breast pang: tobacco was suspected, and the diagnosis was a difficult one; but ten subsequent years of freedom coincident with abstinence from the drug has justified the favourable diagnosis—the diagnosis was established, indeed, in a few weeks, for the patient on giving up tobacco was soon able to convince himself of his soundness of constitution by taking any kind of active exertion without inconvenience.

Tobacco, in common with most kinds of chronic poisoning, tends to produce anæmia; this character should put a smoker on his guard. It is useless to go into the treatment of chronic poisoning by tobacco; there is but one means of cure, namely, to stop the practice of using it in any form. In my opinion he who habitually poisons the structures of his heart is on the way to dilate it, or to produce other statical deterioration of the organ. The way may be a long one, but I have seen many pilgrims far advanced upon it. Even if the patient submit frankly to give up tobacco his heart may long remain irregular; I have reason to suspect that in some cases occurring late in life perfect rhythm is never recovered.

TEA AND COFFEE.—It were an idle thing to write at large upon these articles of common consumption; every housewife may claim to know as much of their virtues as the physician. A few points seem, however, to be worth discussion.

Tea and coffee are nervine stimulants without narcotism. It would seem that in their case the work of the nervous matter is increased directly, not let loose by narcotism of controlling centres, as may be the case with some of the drugs previously described. This stimulation is, as is usual in such cases, followed by exhaustion; according to the degree of the previous stimulation. When taken in moderation, however, this reaction seems either not to be felt, or to be so slight as not to be noticed; the stimulant seems to be clear gain to ordinary persons. In not a few, however, the ill consequences are manifest enough. Another interesting point of distinction is that tea and coffee, unlike tobacco, get no strong hold upon the users of them. A very few persons may find a difficulty in breaking their favourite habit, but even these would be ashamed to admit that they could not do so if necessary.

As also in the case of tobacco, the tolerance of individuals differs very widely. Some persons known to me, in no professional sense, will and do drink strong tea or coffee for breakfast, luncheon, at five o'clock, and again after dinner; and, so far as I can tell, with perfect impunity. Others cannot touch tea even once a day without disagreeable consequences, such as malaise, restlessness, excitement of mind, followed by confusion and depression; and so forth. I think that coffee makes itself felt as an evil more readily than tea, perhaps because it is taken in a stronger infusion or decoction.

Caffeine is a medicine which I have used for many years, and no medicine can be more helpful than this in certain cases, as a diuretic in cardiac or cardio-renal disease, when digitalis and the like have failed, or the patient is getting sickened by digitalis. But I am not now to touch upon the realm of therapeutics. This active principle, common to tea and coffee, is probably the main cause of the insomnia which is due to the use of these articles. But caffeine cannot be the only cause, or even the chief cause, of the other ill effects which follow the abuse of these beverages, because these do not all follow the use of caffeine in its pure state; nor are the symptom-groups in tea and coffee poisoning identical, as they ought to be if the poisonous principles in the two be identical. It seems probable that the aromatic oils, which are obviously very different in the two, are concerned in the disturbance. Caffeine, however, as I have said, is an active agent; and the first effect, especially in the use of coffee, seems to be a rise of arterial blood-pressure, whereby the cerebral activity is stimulated. Tea and coffee thus remove headaches due to cerebral anæmia, as, in a like manner, digitalis will often do.

Tea does not seem to produce the same effects as coffee. I have seen several well-marked cases of coffee excess, and its symptoms are not without character. The sufferer is tremulous, and loses his self-command; he is subject to fits of agitation and depression; he loses colour and has a haggard appearance. The appetite falls off, and symptoms of gastric catarrh may be manifested. The heart also suffers; it palpitates, or it intermits. As with other such agents a renewed dose of the poison gives temporary relief, but at the cost of future misery. Such persons, when assured that the cause of their troubles is coffee, will abandon the use of it without much unwillingness, in which case they are restored to health in a short time. In Watson's language, by renouncing coffee they may get rid of their palpitation and of their apprehensions together. Neither tea nor coffee causes palsy.

Tea likewise affects the heart, but not so promptly and directly as coffee; tea seems rather to affect the brain and the stomach. Many obscure cases of gastralgia are due to tea, and also dyspepsia of the so-called atonic kind. Besides the sleeplessness caused by either drug, tea has appeared to me to be especially efficient in producing nightmare with groanings, startings, and even hallucinations which may be alarming in their intensity. Another peculiar quality of tea is to produce a strange and extreme degree of physical depression. An hour or two after breakfast, at which tea has been taken, at a time when the energies of the system should be at their best, a grievous sinking, referred chiefly to the epigastrium, seizes upon the sufferer, so that even to speak is an effort; the blood seems to leave the lips, and the speech may become weak and vague. Or gastralgia and palpitation, if the malady take that form, may be so acute as to disable the sufferer for a while. Confusion and giddiness may add to his troubles. By miseries such as these a man may find the best years of his life spoilt, unless he find his way to a physician who recognises the cause, and by removal of it sets the patient free. The astringent matters contained in the infusions of tea and coffee promote constipation. The anæmia often seen in such cases is in part indirect, and due to the substitution of tea or coffee for good food. Acne rosacea is said by some writers to arise under the influence of tea and coffee; however this may be, it is wise to substitute cocoa in cases of this affection; for cocoa, so far as I know, is as harmless as it is uninteresting. In out-patient practice in the northern hospitals of England, very obstinate cases of atonic dyspepsia, with sallowness, loss of flesh and low spirits, occur in men in whom no such ailments would be expected. In my experience this malady has especially shown itself in miners and engine-drivers. The state is a grave one, and leads gradually to the loss of working power; so that at fifty years of age such a patient may become both useless and miserable. I was led to believe that this state is largely attributable to the use of tea by the canful; the tea is by no means weak, and too often it takes the place of nourishing food. Unhappily the mischief has often gone too far before the cause is found out and removed.

Dr. Myrtle of Harrogate has repeatedly published his belief that gout is favoured by much tea-drinking. If so, the gout may be an indirect consequence by way of an intermediate dyspepsia.

T. CLIFFORD ALLBUTT.

METALLIC AND SOME OTHER FORMS OF POISONING: INCLUDING POISONOUS TRADES

PHOSPHORUS.—Within the last few years suicidal poisoning by phosphorus has greatly increased in this country, but it is still in Germany and France that the largest number of cases is met with. During the five years ending 1890 there were 36 fatal cases of phosphorus poisoning in this country —14 males and 22 females. Of these 36 cases, 23 occurred in children under the age of five years. The ease with which phosphorus can be procured from lucifer matches by poor people partly explains why this poison is resorted to for suicidal purposes; whilst the knowledge of the terrible suffering which it entails prevents the easier classes from seeking this means of bringing life to a close.[1] There is a varying amount of phosphorus in matches. Roughly speaking, one pound of phosphorus will head 1,000,000 matches. In 100 match-heads Mayet found 55 mgrms. of phosphorus; and Gonning found, in English matches, 32 to 34 mgrms., in Belgian 38. In Munzer's cases each match contained 0·5 mgrm. of pure phosphorus, so that 100 matches would readily cause death; for 7·5 mgrms. (0·116 grain) have proved a fatal dose. Many of the vermin pastes sold in the shops contain as much as from 1 to 2 per cent of phosphorus, and these are always within easy reach of the public.

Commercial phosphorus is obtained from calcined bones by removing the lime with sulphuric acid and deoxidising the residuum with charcoal. It occurs in the form of waxy semi-transparent sticks, which are usually preserved under water. It gives off a peculiar alliaceous odour and takes fire at 100° F. Though usually spoken of as insoluble in water it has been experimentally proved that water dissolves a small quantity of it, that bile has a stronger solvent influence upon it, and that the solubility of phosphorus in each increases with elevation of temperature. It is soluble in bisulphide of carbon, oils, and chloroform. Phosphorus exists in several allotropic forms, of which the red or amorphous is the most common. This form does not take fire at the ordinary temperature, and it is non-poisonous; hence the Swedish matches made with it are harmless. Phosphorus unites with hydrogen to form phosphine or phosphuretted hydrogen—a very dangerous gas.

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[1] In Newcastle-upon-Tyne the number of cases of phosphorus poisoning has been large. In the ten years ending 1894, 50 cases were admitted into the Infirmary, 13 males and 37 females. Of these 50 cases 5 died, 2 males and 3 females. The ages of the patients varied from 9 to 74 years, and with the exception of a child 9 years of age, to whom the poison was administered by the mother, she herself having taken it, the cases were suicidal. So far as the reasons assigned for the suicide are concerned, it appears to me that in the case of men the principal causes are drink and poverty, and in women crossed love or jealousy, poverty, drink, and ill-usage by their husbands.

Phosphorus poisoning may be *acute* or *chronic*. The latter malady, known as *phosphorism*, is principally met with in those who are engaged in the manufacture of matches. Phosphorus, because it is an important constituent of nervous tissue, is administered medicinally in very minute doses, but in these doses its physiological action is different from that of larger quantities. In minute doses it probably acts as a stimulant, improving the nutrition of the tissues, osseous and nervous. Wegner has shown that when adult animals receive small doses of phosphorus the spongy tissue of the bones becomes thickened and the compact portions more dense. New osseous tissue is subsequently developed upon the inside of the shafts of the long bones, in some instances even to the obliteration of the marrow cavity. Therapeutically it is believed that the drug enters the system as phosphorus, not as phosphoric acid; the proof of this is that in cases of poisoning, not only does the breath smell of phosphorus, but the blood is found to contain it. At the temperature of the body phosphorus passes into a state of vapour. Bamberger has demonstrated that in this form it readily passes through animal membrane into defibrinated blood; hence, should phosphorus be present in the alimentary canal, the blood circulating in the walls of the intestine would soon become surcharged with the vapour of it.

Symptoms.—The severity of the symptoms and the rapidity with which they appear depend upon the fine state of division in which the poison enters the body. Under most circumstances the symptoms appear within one to six hours after swallowing the drug; but if a large piece of phosphorus has been taken, symptoms may not arise, for single lumps have been known to traverse the whole length of a dog's intestine without destroying life. In the operation of some poisons there is a marked difference between the symptoms exhibited by animals and by man; but so far as the effect of phosphorus is concerned the symptoms in both are remarkably uniform. On the rapidity of symptoms the condition of the stomach at the time has an important bearing. The presence therein of milk or fat, which readily dissolves phosphorus, causes an early appearance of symptoms. It is not necessary for the poison to be taken internally. Hill reports the case of a girl who, wishing to give a "dark seance" to her fellow-servants, rubbed some phosphorus paste upon her hands and face. The characteristic illumination followed, but the girl died, with the ordinary symptoms of poisoning, on the eighth day.

Tardieu divides phosphorus poisoning into three forms—(i.) the common form; (ii.) the nervous; and (iii.) the hæmorrhagic. In the first form, irritant, nervous, and hæmorrhagic symptoms are blended together; in the second the symptoms are specially referable to the brain and spinal cord, and, as the name implies, hæmorrhages are characteristic of the third.

During the act of swallowing the poison a disagreeable taste and smell are perceived, and are followed shortly afterwards by pain in the gullet and stomach, and by retching and vomiting. The tongue and throat may become red, dry and swollen. In other cases a few hours intervene, during which the patient may move about discharging the ordinary duties of life; and then vomiting and nausea come on, accompanied by abdominal pain. The breath becomes phosphorescent, and the vomited matter, which consists of mucus tinged with blood and bile, may be luminous in the dark and smell strongly of the poison. For two or three days the vomiting continues, accompanied by gastralgia, perhaps by diarrhœa, and by sleeplessness; and the patient meanwhile is utterly wretched. The pulse at this stage may be normal, or feeble and slightly quickened; while the temperature may be normal, or slightly subnormal. By the third day the vomiting usually ceases and the abdominal pain disappears; but this abatement is frequently but temporary, for shortly afterwards—in from 70 to 80 per cent of the cases —jaundice appears on the third to the fifth day, accompanied by coffee-ground vomit and by abdominal pain referable to the epigastrium. The pulse rate may now fall; but if the case is going to take an unfavourable course it may increase in frequency, reaching as high as 150. The temperature varies: a high temperature is generally regarded as a precursor of death; but in some cases observed by myself the temperature before death reached only to 96°. In the vomit numerous reddish brown flocculent masses can be seen; and, on microscopical examination, numerous fat globules, broken-down blood-cells, and débris are observed. The vomit gives a blue colour with peroxide of hydrogen and tinct. guaiaci, indicating the presence of blood. Once jaundice supervenes, the patient can no longer be regarded as simply under the influence of phosphorus, but as suffering from the consequences of the profound structural changes in the liver which are induced by the action of this substance upon the hepatic cells. The viscus, at this stage, may be somewhat enlarged and tender; but if the patient survive, the liver becomes rapidly smaller, so much so as to suggest, in the absence of a history of phosphorus poisoning, the diagnosis of acute yellow atrophy of that organ. The urine may be scanty, usually it is about the average in quantity; it may be albuminous and loaded with biliary colouring matter: it frequently contains crystals of leucin and tyrosin. The headache and sleeplessness complained of in the first few days may now be replaced by delirious excitement and convulsions: these gradually give way to coma, preceded by a marked declension of the temperature. Occasionally, in the early stage, when the vomiting abates there is a remission of the symptoms; and it seems as if the patient would recover, but in due course jaundice supervenes. When recovery takes place the amount of poison swallowed has been small, a successful line of treatment has been adopted early, or the phosphorus has become oxidised in the intestinal canal. When the poisoning is fatal, death may not come for several days; but in the case of children it may happen within the first twenty-four hours, so that the stage during which jaundice usually occurs may never be reached.

In Tardieu's second form of phosphorus poisoning the symptoms are referable from the outset to the nervous system. Not only are there vomiting and abdominal pain, but peculiar sensations in the limbs also, followed by cramp-like pains or paralysis, and by delirium and convulsions with or without jaundice. Gallavardin quotes the case of a matchmaker in Sweden who, after inhaling the vapour of phosphorus consequent upon an explosion in the works, suffered from gradual paralysis of the limbs with trembling of legs, arms and hands, and paralysis of the tongue, causing embarrassment of speech.

The skin, in addition to being icteric, may become the seat of erythema or small hæmorrhages; blood may ooze from the intestinal mucous membrane or from the kidney. Jaundice may occur at any time after the first day. The rapidity of its manifestation is a measure of the danger to life; the liver becomes enlarged and tender at the same time, the enlargement being generally uniform. Ingravescent jaundice gives rise to a series of nervous symptoms (delirium, coma, and convulsions) akin to cholæmic intoxication, and is followed by rapid death. On the other hand, the jaundice may gradually disappear, the appetite return, the abdominal pains cease, and recovery, in a few weeks, be fairly complete.

Opinions differ as to the state of the blood, probably because they have been founded too much upon experimental data. Munzer found the alkalinity of the blood diminished owing to increased production of acids within the body; and, on microscopical examination, that both the red and white blood cells were normal. He believed, nevertheless, that the red blood cells were increased in number, a circumstance which many authors regard as a primary result; though the secondary effect of the continued use of phosphorus is to cause a diminution of the coloured discs. The blood is frequently dark, and not so liable to coagulate as in health.

The urine is almost invariably affected in phosphorus poisoning. In the early stage it may contain a trace of albumin; but when jaundice arises it contains in addition bile pigments and urobilin or reduced bilirubin. Sugar is generally absent. Hyaline tube-casts may be observed, with or without fat droplets or fatty crystals; or tube-casts composed of fatty renal epithelia mostly stained with bile, and sometimes mixed with the débris of broken-down red blood cells. When tyrosin is present it indicates that important changes have already taken place in the liver—that it is the seat of fatty degeneration, and is beginning to atrophy. Hæmatoidin crystals have been found in the urine by Munzer, as well as certain acids—for example, the sarcolactic. During the stage in which jaundice is present the urine is not necessarily decreased in quantity, but its specific gravity is raised and its reaction is acid. A transitory peptonuria may occur. Von Jaksch states that in the earliest days of phosphorus poisoning there is a fall in the total nitrogen eliminated, and that this is followed by a rise. As early as the third day I have observed a very decided diminution in the daily discharge of urea; and this may continue for several weeks in patients who ultimately recover, without any reduction in the amount of urine passed. In fatal cases there is a rapidly progressive fall in the urea, and this becomes well marked the day before death. Some authors maintain that the quantity of uric acid in the urine is slightly increased throughout the illness, also the ammonia. Munzer believes that the excessive ammonia plays a useful part in the organism by neutralising the abnormal acid products formed by the action of phosphorus upon the tissues. The amount of phosphoric acid in the urine is increased during the early period of the poisoning, but in unfavourable cases it subsequently sinks below the normal; a similar fate befalls the sulphuric acid. When the jaundiced urine from a case of phosphorus poisoning is kept for a time it emits a strong garlicky odour which is increased on adding nitric acid.

When jaundice appears the fæces become pale and contain fatty matter and crystals; they may contain phosphorus and emit its characteristic odour.

Women, if pregnant, usually miscarry after taking a fatal dose of phosphorus. In a case recently under my own observation the woman, who was eight months pregnant, miscarried on the third day; the child was still-born. Labour under these circumstances pursues the usual course; but within two or three days afterwards jaundice appears and gradually deepens in tint; the liver becomes more tender; somnolence increases, and the patient gradually dies comatose. Phosphorus frequently produces a bloody discharge from the uterus. In the dead fœtuses expelled by rabbits that have been experimentally poisoned structural changes are met with similar to those observed in the mother. The mortality rate is very high amongst the children of parents engaged in the manufacture of matches and tainted with phosphorism.

Forty per cent of cases of acute phosphorus poisoning die. It is no uncommon thing for apparently slight cases to change for the worse; and even after the jaundice has disappeared and the symptoms generally have improved, sudden death may occur by failure of the heart from fatty degeneration. A tardy development of jaundice is a favourable indication, particularly if it be slight and unaccompanied by enlargement of the liver. The retention of the appetite is a favourable prognostic indication. On the other hand, an early appearance of jaundice, and the appearance of such nervous symptoms as convulsions and coma, a rapid, small and irregular pulse, considerable enlargement of the liver, the presence of hæmorrhages, and an increased temperature, betoken an unfavourable termination.

The diagnosis of phosphorus poisoning is only certain when in the vomited matter or fæces phosphorus is found. The illness may be mistaken for—(*a*) Acute yellow atrophy of the liver; (*b*) Rapidly developing hypertrophic cirrhosis ending fatally by cholæmia; (*c*) Certain forms of sepsis; (*d*) Certain forms of eclampsia; (*e*) Morbus Weilii; (*f*) Hæmorrhagic small-pox; (*g*) Obscure forms of alcoholic and uræmic intoxication.

In acute yellow atrophy of the liver there is a greater tendency to brain disturbance, and also to enlargement of the spleen, than in phosphorus poisoning. The liver, too, decreases rapidly in size, the jaundice meanwhile deepening; whereas in phosphorus poisoning the jaundice appears with enlargement of the liver and runs parallel with it, although in a certain number of cases this organ subsequently shrinks, when the two diseases have a greater resemblance. In acute yellow atrophy the urine frequently contains so much leucin and tyrosin that on the addition of a few drops of acetic acid a dense precipitate is thrown down.

Occasionally hypertrophic cirrhosis of the liver appears rather quickly, and leads to rapid death by cholæmia. Upon one differential symptom between this disease and phosphorus poisoning von Jaksch lays considerable stress; namely, the regularity with which during the last few days of life in hypertrophic cirrhosis vomiting of brown sanguineous material occurs; but in my opinion this is not a trustworthy guide. The duration of the illness and the history of the case rather deserve attention. Cases of puerperal eclampsia with an icteric tinge might be mistaken for phosphorus poisoning; but in these the temperature, although irregular compared to the transitory pyrexia of the other illness, is generally high and persistent. Besides, the liver is usually not enlarged. Dropsy if present would be an aid in the diagnosis. The amount of albumin in the urine and the tendency for it to contain blood are greater in eclampsia.

Certain forms of alcoholic and uræmic intoxication resemble phosphorus poisoning, and are with difficulty distinguished. In all doubtful cases the vomit should be carefully examined. In hæmorrhagic small-pox the persistently high temperature would be a guide. In Weil's disease the symptoms begin suddenly, usually with a slight rigor; the pyrexia, which is higher than in phosphorus poisoning, lasts for eight or ten days accompanied by headache; and we find also gastric disturbance, jaundice, pains in the calves, enlargement of liver and spleen, nephritis and erythema—a group of symptoms closely resembling those met with in phosphorus poisoning. The prognosis of Weil's disease is favourable. The proof of poisoning, on the other hand, rests upon the detection of phosphorus in the vomit, in the rinsings of the stomach, and in the fæces; and there are several methods by which this may be accomplished. In Mitscherlich's process for the detection of phosphorus the vomit is distilled with sulphuric acid in the dark. The retort is connected with a glass condenser, and if phosphorus be present luminous rings appear at the point where the fumes come into contact with the cold water. In the method known as Scherer's the vomit is enclosed in a flask with an air-tight stopper; and two test papers are placed therein, one saturated with nitrate of silver and the other with acetate of lead: should phosphorus be present, the silver paper is blackened whilst the other remains unchanged. In the urine from a case of phosphorus poisoning leucin and tyrosin may be found—the former as little round or oval spheres not unlike droplets of fat, and the latter as heaps of delicate needle-like crystals. The best chemical test for tyrosin is to dissolve the sediment in hot water, and to add a drop of a solution of mercurous and mercuric nitrate (Millon's reagent), when if tyrosin is present in minute quantity a rose colour at once appears, and a crimson precipitate if there be more than a trace. For a good method of separating leucin and tyrosin the reader is referred to Wynter Blyth (5).

Morbid anatomy.—The cases must be few in which no lesion is found after death; the character of the morbid changes depends upon the rapidity of the poisoning and the manner in which phosphorus entered the system. Usually there are numerous ecchymoses on the skin, on the serous and mucous membranes, and in the muscles and adipose tissue. In a case recently seen by myself there were numerous small hæmorrhages under the visceral layer of the pericardium. The blood is liquid and dark. If death occurred in the early stage there may be a distinct smell of phosphorus. The skin is jaundiced. There is inflammatory redness of the stomach, with swelling or hæmorrhagic erosion of the intestinal mucous membrane. The liver is increased in size in the early stages; diminished if the illness was protracted; it is of a uniform citron or greenish yellow colour, or it exhibits irregular yellow patches; on section it is bloodless. The gall-bladder may be full or empty. The kidneys are large and their cortex pale, but the medullary portions are congested. The spleen is not enlarged. On microscopical examination is seen very marked fatty degeneration of the liver-cells and of the renal epithelia. The muscle-fibres of the heart have lost their transverse striation and contain numerous fat droplets—a change also observed in the voluntary muscles. Beyond an occasional hæmorrhagic point or two, from increased permeability of the capillary walls, and vacuolation of the nuclei and cells in the cerebral cortex, there is nothing to be detected in the nervous system. Lilienfield and Monti describe a micro-chemical method for detecting phosphorus, which consists in placing sections of the fresh organ in strong solution of ammonium molybdate, and transferring them in half an hour to a 20 per cent solution of pyrogallic acid dissolved in ether. After remaining for a few minutes they are passed through spirit to oil of cloves, and then mounted in Canada balsam. A yellow or brown colour, best marked in the nuclei, indicates the presence of phosphorus. Overlach found in acute phosphorus poisoning of unimpregnated animals, that certain well-defined changes occurred in the uterine mucous membrane closely akin to those met with at normal menstruation: there was a development of large cells, resembling the so-called "decidual cells" of pregnancy, from the interglandular connective tissue.

Treatment.—As the main object is to prevent absorption of the poison, emetics and purgatives must be given at once; for once absorption has taken place it is difficult to control the consequent organic changes. If the case is seen early an emetic of sulphate of copper should be given, and the stomach persistently washed out until there is no longer any smell of phosphorus. Objections have been raised to the employment of copper sulphate on the ground that it causes gastro-enteritis; but there is little chance of this occurrence if it is given in from 3 to 5 grain doses, freely diluted, every few minutes. Black phosphide of copper is thus formed, which is harmless and readily eliminated by the kidneys. The washing out of the stomach may be accomplished with warm water containing copper sulphate, and subsequently with calcined magnesia. This line of treatment may suffice alone; but for the next few days it is necessary to forbid all fatty foods, excluding even milk and eggs, for fat dissolves any phosphorus left in the stomach. Other lines of treatment have for their object the oxidation of the phosphorus so as to render it inert, as, for example, the use of peroxide of hydrogen, a drug which is too unstable to be trusted. Duplos suggested liquor chlori, and Scherer chloride of lime; but experience has shown that they act too slowly. Potassium permanganate freely diluted is a safe and fairly trustworthy oxidising agent, but it must be given early. Oil of turpentine is the antidote usually employed; for its use we are indebted to Andant, who in 1868 was called to see a man who had attempted suicide by swallowing phosphorus paste, and to hasten the end had subsequently drunk turpentine. To the astonishment of both doctor and patient, not only were the symptoms slight, but the patient recovered. Bush of Dorpat has experimentally demonstrated how turpentine delays the toxic effects of phosphorus; and of fifteen dogs similarly poisoned by Personne, ten, to which turpentine was administered, recovered, while the remaining five died with the characteristic symptoms. Apart from its stimulating properties, it is maintained that phosphorus forms with turpentine a crystalline mass like spermaceti; but the only kind of it which is capable of doing this is the old French oil of turpentine, now with difficulty obtainable. The other two forms of turpentine—namely, the rectified and the German—have been shown by Vetter in his experiments upon dogs and rabbits to be useless. Ordinary commercial oil of turpentine in forty-drop doses, after the stomach has been washed out, still remains, however, a favourite line of treatment; and a fairly large percentage of cases thus dealt with recover. The efficacy of turpentine is increased by long exposure to the air. It is very desirable that the bowels should be cleared out by enemas or by gentle saline aperients.

Industrial phosphorus poisoning.—The number of people engaged in the manufacture of phosphorus in this country is small, probably not more than 100; and as the greater part of the process is carried on under water there is no great risk to health. The most important industry in which phosphorus is largely used is in the making of lucifer and other kinds of matches. It is estimated that in England this industry gives employment to 2500 people. Phosphorus enters into the formation of ordinary wooden or congreve matches, wax vestas, and vesuvians. Certain departments in the manufacture are more injurious than others. The "composition" into which the ends of the matches are dipped contains phosphorus, potassium chlorate, and glue; and, occasionally, powdered glass, sulphide of antimony, manganese peroxide and colouring matter. Not more than 5 per cent of phosphorus need be present in the composition. It is in the "mixing" of the composition, and in the "dipping" and "drying" of the matches, that noxious fumes are given off. In the manufacture of "safety" matches and in matches that come from Sweden no yellow phosphorus is employed. For ignition these matches have to be rubbed on a portion of the box covered with a dried paste, the principal ingredient of which is the harmless red or amorphous phosphorus. The entrance of phosphorus fumes into the system by way of the respiratory organs is followed by a slow intoxication called in France *phosphorism*, of which cachexia, a yellow tint of the skin, garlicky odour of the breath, the presence of phosphorus in the urine and saliva, anæmia, abortion, a high rate of infantile mortality, albuminuria, and demineralisation of the tissues, are the most important symptoms; to these may be added cystitis, bronchitis, rupture of the muscles and fragility of the bones.

Amongst matchmakers one of the most serious consequences of the prolonged exposure to phosphorus fumes is disease of the jaw-bone. The work-people suffer from necrosis of the bone, sometimes called in this country "phossy jaw," and in France "mal chimique"; a disease which attracted considerable attention in Germany and Austria so far back as 1838, and which in our own country of late has been the subject of a departmental Government inquiry. The "mixers" and "dippers" are particularly liable to suffer from phossy jaw. The disease, though it affects both jaws, yet principally affects the lower; and the first symptom of it is toothache, which is not relieved by extraction. We cannot say definitely how phosphorus fumes act upon the bones. By some it is supposed that arsenic, which is frequently present with the phosphorus, causes the inflammation. Wegner experimentally produced necrosis of bone by the direct action of phosphorus fumes upon those portions where the periosteum had been exposed by dissection. Hence the greater liability for those persons to suffer who have carious teeth. It is supposed that the fumes enter the carious cavity and reach the peridental membrane by the apical foramen (103). Operatives with decayed teeth have always been regarded as specially susceptible; although it has been lately maintained that the local inflammation is part of a general poisoning of the system. Mr. Hutchinson mentions a case where the prolonged internal use of phosphorus was followed by a typical necrosis of the jaw. Mears found that in the early stages of phosphorus necrosis there is an accumulation of tartar round the neck of the teeth, and that the disease is a chronic toxæmia with local irritation of the gums aggravated by decayed teeth and tartar. Cold readily excites inflammation in such gums, and this extends to the periosteum. Mears also noticed that the gums of cachectic operatives are the seat of small hæmorrhages. He considers that the poison enters the system by inhalation and also with the food, and that the toxæmia precedes the local affection; hence such primary symptoms as nausea, vomiting and increasing debility. Beginning as an inflammation of the gum accompanied by toothache, or as inflammation of the peridental membrane, it gradually extends to the periosteum, along which the process advances until a large part of the bony covering of the jaw is affected. This is followed by an osteomyelitis which ends in necrosis. As each tooth in the early stages is removed on account of pain it often happens that a small quantity of pus escapes from the alveolar cavity; the pus as it escapes frequently has the odour of phosphorus. The teeth become affected one after another until a large portion of the jaw is denuded of its periosteum.

François Arnaud, from his position as medical officer to the match factories of Marseilles, has had unusual opportunities of studying the disease known as chronic phosphorism. Matchmakers, he says, are readily recognised by the peculiar odour which hangs about them and escapes by their breath. So strongly has their system become impregnated with the poison, that practically speaking all their excretions exhale an alliaceous odour. As might be expected, the prolonged elimination of phosphorus by the kidneys is followed by albuminuria in a large percentage of those whose work most exposes them to the poison. Their health, notwithstanding, does not deteriorate rapidly. The garlicky odour of the urine is regarded as a measure of the amount of the poison present, for it is as free phosphorus that this substance appears in the urine. Arnaud has never noticed the phosphorescence of the urine in the dark of which some observers have spoken. Urea is generally high, but phosphoric acid is not increased in quantity—this, as we have seen, is not the form in which phosphorus leaves the kidneys. Phosphorus appears so to act upon nutrition generally that if work-people are in good health metabolism is stimulated thereby; and not only is the amount of urea in the urine increased, but the inorganic constituents as well. Should anything arise, however, to disturb elimination, or should dental defects appear, the toxic effects of the element gradually manifest themselves.

Exposure to phosphorus fumes is doubtless the exciting cause of this malady; but, as already mentioned, depressed general health, an unwholesome condition of gums and teeth, and ill-ventilated workrooms dispose to it. Improved ventilation, reduction of the amount of phosphorus in the "composition," wearing of respirators in the drying-room, dismissal of all work-people who have bad teeth or who suffer from inflammatory affections of the gums, personal cleanliness of the workers, careful washing before eating, and the provision for meals outside the factory, are precautionary measures of the greatest importance. We should not aim, however, at the prolongation of so harmful an industry; as the substitution of the amorphous for the yellow phosphorus, or the manufacture of matches by machinery, in strictly confined spaces whence little or no emanation can escape, will avert the evil.

The treatment of phosphorism and its cachexia should be directed towards the elimination of the poison. Exclusive milk diet, the inhalation of oxygen, gentle exercise, and repeated small doses of turpentine, are the agents recommended by Magitot of Paris, who has had a large experience of the disease amongst the French matchmakers. In American factories the operatives, believing that turpentine vapour neutralises the fumes of phosphorus, carry wide-mouthed vessels containing the oil suspended by straps round their neck. The gums of the work-people should be regularly examined, and the presence of the slightest change therein should oblige the operative to cease work, and to use a mouthwash of boracic or carbolic acid. Once suppurative periostitis is established an effort should be made to limit it by free incision and thorough drainage—washing out the sinuses with weak corrosive sublimate or carbolic acid—and giving the patient good food; still when this stage is reached necrosis is almost sure to follow. Although resection is the proper treatment for the necrosed jaw, surgical interference should be avoided so long as profound phosphorus cachexia remains; operation under these circumstances is very apt to be followed by a recurrence which the surgeon cannot always control.

MERCURY.—Workers in mercury become poisoned by direct handling of the metal, by breathing it in the form of vapour or dust, or by absorption through the skin. When mercury is continually handled it tends to throw the skin into creases, within which fine particles of the metal become lodged and subsequently absorbed. Eating with unwashed hands conveys metallic particles into the gastro-intestinal tract, where, under the influence of the digestive juices, they become dissolved. The mercury used in this country comes from Spain as cinnabar or sulphide. From cinnabar the pure metal is extracted by simply roasting the ore alone, or by mixing it with lime or iron filings, when metallic mercury is given off which readily condenses. This process of extraction is dangerous to those employed. Work-people exposed to mercurial vapour at a low temperature scarcely suffer: the danger increases with elevation of temperature; for having penetrated into the respiratory passages, the vapour, as the temperature falls, becomes condensed, and forms small droplets or granules which are deposited on the mucous membrane. When, on the other hand, the temperature in the workshop is low, the mercury, too heavy to remain suspended in the atmosphere, is deposited on the hair or beard of the workman, or upon his hands and clothes; and with this upon him he leaves the factory. Men who handle the metal, or who are engaged in the preparation of its salts, also run the risk of being poisoned by absorption through the lungs, creases or cracks in the skin, wounds, or the open sores which are the effects of the mercury. Add to these the habitually diseased condition of the gums, to which Galippe drew attention, and the channels by which the poison may effect an entrance are many. Until lately water-gilders made use of mercury for depositing gold on metallic surfaces; and in mirror-silvering it was also employed. Water-gilding in this country has been largely replaced of late by electro-plating. The silverers used to suffer considerably from mercurialism; but the silvering of mirrors, which is still an important industry, is now practically harmless to those employed in it, since the process by which metallic silver can be deposited on glass from the metallic tartrate has come into use. In barometer making, bronzing, felt-hat making, skin and fur dressing, mercury, or its salts such as the bichloride and nitrate, is used; and poisoning occurs occasionally. One of the most frequent consequences of industrial mercurialism is tremor of the limbs; and this, usually the consequence of breathing mercurial vapour, may be the only manifestation of any effect upon the system. If work-people are exposed to the vapour at a high temperature, tremor is rapidly induced; hence the readiness with which it attacks those who are engaged in smelting the metal or in making amalgam. Eight per cent of the men thus employed suffer. Certain conditions have long been known to dispose to this form of poisoning; for example, want of cleanliness on the part of the artisan, deprivation of food, and the abuse of alcoholic stimulants. As far back as the early part of this century Merat denounced the uncleanly habits of gilders, and earlier still Jussieu demonstrated that the convicts engaged in the mines of Almaden, and who lived continually therein, became a ready prey to mercurial tremor; the free miners, on the other hand, who lived in the neighbourhood, who were careful to exchange their clothing, and to eat only after washing, enjoyed health as good as other people in the district. Authors who have subsequently written upon the conditions of life at the mines of Almaden repeat this story. As late as 1886 Raymond, who had visited the mines, states that the work-people possessed of a good constitution, who follow agriculture after their mining is done, and who lead regular lives, are almost never attacked; and if they are, then health is soon regained by desisting from work in the mine for a time.

In the ten years ending 1892 there were 59 deaths from mercurial poisoning in England—40 males and 19 females; of these, 16 males and 18 females were cases of suicide, mostly from corrosive sublimate.

Symptoms.—The tremor, which may appear suddenly or slowly, is at first observed on movement only; but ultimately it becomes constant. It is usually limited to the arms, and is confined to certain groups of muscles. In some of the very severe cases the tremors may be so violent as to resemble violent chorea. The patient prefers to lie on the floor; he can neither clothe nor feed himself, and it is with difficulty that he gets more than short snatches of sleep, during which the trembling disappears. The powers of speaking, chewing, and walking are affected. In addition to the tremor there are frequently stomatitis with abundant salivation, and symptoms of gastric catarrh and diarrhœa followed by emaciation and paralysis. As the salivary glands, so the pancreas, seems to be readily influenced by mercury; hence the watery character of the stools and the large, congested condition of this organ found after death. In some cases there is "wrist-drop," as in plumbism; a condition due, says Letulle, to degeneration of the sheath of peripheral nerves, the axis cylinders remaining healthy.

Gingivitis, profuse ptyalism—the saliva being secreted to the extent of from one to two gallons a day, fœtid breath, ulceration of the interior of the cheek with sloughing followed by cicatrisation or periosteo-alveolar swelling, fungous gums, decay and shedding of the teeth, conjunctivitis and cachexia are observed in industrial mercurialism. Excessive salivation is frequently accompanied by a slight rise of temperature; and its progress is favoured by the existence of disease of the kidneys. The cachexia, which resembles that of scurvy, is characterised by great anæmia, debility, emaciation, loss of hair, pains in the muscles and joints, and œdema of the feet. There is a reduction in the number of the coloured corpuscles and in the albumin of the blood. Periostitis and enlarged glands may be consequent upon the state of the gums; and there may be skin eruptions of the nature of erythema, or eczema, followed by desquamation. Individuals thus affected frequently succumb to phthisis. The cerebro-spinal system may become affected; the patient may complain of sleeplessness or giddiness, or of epileptiform seizures and paralysis—the paralysis differing from that met with in plumbism, in the persistence of the normal electric contractility of the muscles, the axis cylinder of the nerves not being destroyed: the diagnosis is corroborated by the absence of a blue line on the gums, and the history of the occupation of the patient. The tremor resembles that observed in disseminated sclerosis and paralysis agitans. In disseminated sclerosis and in mercurialism the tremors appear during exertion, and cease when the patient is at rest or asleep; those occurring in hydrargyria are less wide and irregular, they are not accompanied by nystagmus, but by more pronounced stammering in speaking. In both diseases the tongue, when protruded, is tremulous. In paralysis agitans, on the other hand, the tongue is steady when protruded, and there is little or no oscillation of the limbs during effort; the tremors are observed even when the patient is at rest, they affect the wrist and fingers particularly, and the patient exhibits a peculiar forward gait, impelling him to pass from a walking to a running pace. As a distinguishing feature between mercurial tremor and that occurring in disseminated sclerosis Charcot pointed out that while the oscillations cease during rest it is in the former case in a remittent manner only; and they reappear from time to time without the patient making any movement spontaneously or under the influence of emotion; whereas in insular sclerosis the tremor is completely absent during rest (12). There is also a superficial resemblance between mercurial tremor and general paralysis of the insane. In the latter the tremor is never so pronounced; moreover the inequality of the pupils, the grandiose ideas, and the symptoms of spinal degeneration are not observed in mercurialism. Generally speaking, it is upon the nervous system that the poison exerts its most baneful influence. Two young men, assistants in the chemical laboratory at St. Bartholomew's Hospital, suffered severely after making mercuric methide. Besides emaciation and paralysis of motion and sensation, symptoms of acute mania set in, in the course of which one of the sufferers died; while the other, who never thoroughly regained his health, died a few months afterwards from pneumonia. Symptoms resembling hysteria may be met with, but these occur in people with a proclivity thereto; whilst in other cases vertigo, hallucinations, and insanity—a condition spoken of as "mercurial erethism" (Gowers)—mark the invasion of the cerebrum. Removal of the individual from the influence of the poison may be quickly followed by a subsidence of the acute symptoms. By the various emunctories mercury is eliminated from the system; nevertheless the process may be slow and extend over years. Kussmaul states that the children of workers in mercury are anæmic and ill-nourished; and that they frequently suffer from rickets and phthisis: also that women, if pregnant, miscarry and that the infant is still-born. Baumler quotes the case of a man—a gilder—who, after following his occupation for twelve years, was obliged to desist on account of tremor, loss of memory, shedding of teeth, and so forth. He married three times. All his wives followed the occupation of gilding. By his first wife he had four children: one died of gangrene of the feet; the other three and the mother died of phthisis. By his second marriage he had two children, who, with the mother, died of phthisis. By the third union all the children born before the mother took to gilding remained well; but the one born subsequently died from a cause not stated, although the mother died of phthisis (59). In "sole stitching" by American machinery the men are said to have become mercurialised by volatilisation of the metal.

Improved ventilation of the workroom will diminish industrial mercurialism; and to this precaution may be added the use of sulphur baths, careful scrubbing of the body with soap and water, rinsing the mouth with chlorinated water, brushing the teeth, and the wearing of respirators containing a sponge that has been dusted with sulphur, or soaked in a dilute solution of silver nitrate. Iodide of potassium in small doses is regarded as a prophylactic, but it easily causes iodism. The internal administration of sulphur and plenty of milk are useful preventives.

Upon animals, as upon man, mercury exercises an injurious influence when applied to the skin; salivation and stomatitis occur, followed by paralytic phenomena. It has generally been supposed that when the metal is pure and swallowed in bulk it is non-poisonous; but in a case alluded to by Wynter Blyth tremor and loss of muscular power were seen. Occasionally profuse dermatitis, with desquamation, has been the consequence of administering mercury, therapeutically, by the skin: death, indeed, has followed the practice. The symptoms of mercurialism may be met with in any person, no matter by what channel the metal entered the system. In the case of the corrosive salts of mercury—for example, mercuric chloride or corrosive sublimate—the symptoms are immediate and very severe. Three grains have proved fatal. Death may occur within twenty-four hours. The patient complains of a sense of burning heat in the throat with a sense of constriction in the act of swallowing; the mucous membranes look pale and shrivelled as if they had been brushed with lunar caustic. Œdema of the glottis rapidly comes on, followed shortly after by death from asphyxia: or there is severe epigastric pain accompanied by repeated vomiting streaked with blood, and diarrhœa with bloody stools. The temperature quickly falls, the breathing becomes difficult, the pulse small and irregular, the urine scanty or completely suppressed; collapse supervenes, and death, which may or may not be preceded by convulsions, occurs. After death the whitened escharotic condition of the gastro-intestinal mucous membrane is very noticeable, with here and there ecchymoses and black patches due to the deposit of sulphide of mercury.

Similar symptoms have followed the internal administration of mercuric nitrate and its external application to the cancerous womb; and the more recent and extensive employment of the bichloride of mercury, as an antiseptic in abdominal surgery or as a uterine douche in midwifery, has been followed by symptoms of an extremely dangerous character. Of the antiseptic value of bichloride of mercury there is no doubt. Koch has demonstrated that 1 in 1000 parts of water will destroy the most virulent of germs in non-albuminous media. If albumin be present this becomes coagulated, and an albuminate of mercury is formed and deposited which leaves the supernatant liquid free from the drug, and therefore without antiseptic power. Laplace, one of Koch's assistants, has shown that this accident may be averted by the addition of a small quantity of acid. The acid sublimate is therefore the surest and most powerful antiseptic. In a solution so weak as 1 in 50,000 it is capable of destroying the microbes of pus.

Prevost has published the results of his experiments upon animals with various salts of mercury, administered subcutaneously or given by the mouth. The results, if the dose was fairly large, were diarrhœa, great debility, albuminuria with tube-casts, hæmaturia, collapse, and death within a few hours. When the dose was smaller the symptoms were the same, but less severe; they were accompanied by rapid emaciation and death within a few days. As in arsenical poisoning, the symptoms appeared equally when the mercury was injected subcutaneously or given by the stomach; but a smaller dose sufficed when given hypodermically. In some of Prevost's animals death supervened within a few hours after the subcutaneous injection of the peptonate of mercury, and was apparently due to paralysis of the heart; as the end came before there was time for any lesions of the internal organs. The blood, too, was dark and diffluent, similar to that observed when arsenic, platinum, or silver nitrate has been injected. In Mering's experiments the kymograph registered a very rapid and progressive fall of the arterial pressure, even after the administration of atropin or section of the vagi—a proof that the diminished arterial pressure was due to cardiac failure.

Morbid anatomy.—The internal lesions to which Prevost draws attention deserve notice. By whatsoever channel the mercury was administered, the intestine generally contained large quantities of liquid of a yellow-brown or sanguinolent character; the bloody matter being most frequently found in the neighbourhood of the cæcum and in the large intestine. There was extensive desquamation of the mucous membrane of the small intestine and cæcum, with hyperæmia and ecchymoses. It is difficult to explain the intestinal hyperæmia in metallic poisoning. Is it due to altered blood-pressure, the existence of which Mering demonstrated, or is it due, as Roy's experiments upon colchicum suggest, to an elimination of the mercury by the intestinal mucous membrane? The latter is the more likely explanation.

In one of Prevost's cases, that of a man poisoned by mercuric nitrate, the kidneys were the seat of a peculiar form of nephritis. The epithelial cells of the convoluted tubules were granular and opaque; in places the tubules were filled with compact masses composed of chalk. In subacute cases of mercurial poisoning a decalcification of the bones occurs with a deposit of lime salts in the kidneys.

Although large doses of mercury cause deterioration of health, in very small doses the drug seems to act as a stimulus to nutrition. Many patients in my experience put on flesh when taking mercury; and their blood-making organs have their functional activity increased, as witnessed by the larger number of red blood cells.

Mercury is eliminated by the kidneys and saliva, and by the milk of nursing women; whilst its insoluble salts pass out by the bowels. Like lead it is supposed to enter into combination with albuminous bodies in the tissues, there remaining inert, to be subsequently oxidised and returned to the circulation as an active poison. Mercury has been found in the urine and saliva two and four hours respectively after having been swallowed, and in the urine fourteen hours after having been applied to the skin. Although it is said to be thrown out of the system entirely and with some rapidity, mercury has been found in the brain, liver, muscles, and kidneys of animals. It is probable, therefore, that while a single dose of mercury is rapidly eliminated from the system, repeated small doses distributed over a long period are not regularly eliminated; hence more or less of it is deposited in the tissues.

Mercury is detected in organic substances and fluids by what is known as Ludwig's method. Urine is evaporated to dryness and then treated with hydrochloric acid; or the urine may be simply acidified and then heated to 50°-60° C.: the suspected tissues are cut small and boiled in 20 per cent hydrochloric acid. To these granular zinc or finely-divided copper is added, and the whole is shaken up well and then allowed to settle. After pouring off the supernatant fluid the sediment obtained upon a filter is well washed with boiling water and dried at 60° C. It is then placed in a combination tube of hard glass and covered with a plug of asbestos, upon which is placed a layer of granular oxide of copper. Another asbestos plug and layer of zinc previously dried and heated may be added. The tube is now drawn out into a thin capillary extremity and combustion made. The mercury is deposited as a metallic powder in the capillary tube. This portion is now broken off and a few particles of iodine placed in it whilst it is still hot. As the iodine vapour impinges upon the mercury scarlet mercuric iodide is formed which is at once recognisable by its colour. A readier test, after boiling with hydrochloric acid and water, is to place a piece of pure copper foil in the tube while the liquid is warm; if left for several hours it acquires a silvery lustre, from which globules of mercury are to be obtained by sublimation.

Treatment.—Ptyalism is relieved by mouth-washes of myrrh and potassium chlorate, with tonics internally. The treatment of acute mercurial poisoning consists in encouraging the vomiting, usually present, by means of apomorphine in four-drop doses hypodermically administered; or by sulphate of zinc given by the mouth. Generally the vomiting is such that these emetics are unnecessary, as also the use of the stomach-pump, so needful in other forms of poisoning. Under all circumstances the administration of diluent drinks containing white of egg is called for. If there be much pain, opium or morphine may be given. In the slow forms of poisoning the symptoms must be dealt with on general principles. The nutrition of the system must be carefully attended to. Potassium iodide may favour the elimination of the poison. For mercurial tremors phosphide of zinc in pill form, $\frac{1}{10}$ to $\frac{1}{4}$ of a grain, is recommended to be taken twice or thrice daily.

COPPER is widely distributed in nature. It is found in several soils and in spring and river water; occasionally in wheat and turnips, in other articles of food and drink, and in the blood of several of the invertebrates. According to Dupré it is frequently present in small quantities in the liver and kidneys of man, but more particularly of ruminants. The use of copper cylinders and boilers in cooking is one source by which food and drink may become adulterated. Salts of the metal are occasionally employed to impart a green colour to preserved vegetables, such as green peas, so as to render them attractive to the eye; and in France they are added to absinthe to improve its colour. Cupric sulphate is administered internally as an emetic; it is given in very small doses as a tonic to the nervous system, and is used in diarrhœa as an astringent. Applied in a weak solution externally to wounds it acts as a stimulant and astringent; but beyond these purposes the metal is little employed in medicine. A considerable amount of copper is present in ordinary bronzing powders; and it is a large ingredient of the powders which are used for the lilac and purple fires of the pyrotechnist. Horses and cattle can take large doses of sulphate of copper (2 drachms) without any apparent bad effects; but the same quantity has caused very serious symptoms in the human subject. When administered by the mouth it acts as an irritant poison, causing violent and persistent vomiting, depression of temperature, and death from respiratory failure; but when given hypodermically vomiting is not induced.

Symptoms of copper poisoning in man appear shortly after the drug has been swallowed—in from one quarter of an hour to two hours: these are, a metallic taste in the mouth with salivation, severe vomiting of green-coloured matter, colic and purging; the stools contain glairy mucus and blood, and if the dose has been large, death follows these symptoms in a few hours. It is often preceded by convulsions and delirium, paralysis, syncope, scanty or suppressed urine, and hæmoglobinuria. Should a fatal termination be warded off for the time being, jaundice, followed by great nervous depression, may supervene. In fatal cases there is well-marked gastro-intestinal inflammation with numerous ecchymoses; and the liver is observed to be fatty.

In the **treatment** of acute copper poisoning milk and eggs are efficient antidotes. Eggs should be beaten with water or milk and administered freely so long as vomiting continues. The alkali which is present in soap renders this commonplace article also useful as a means of treatment. Pure prussiate of potass precipitates copper from its solutions, and in small doses may prove beneficial. After antidotal treatment has been tried, opium in small doses may be needed for the relief of pain.

As an **industrial disease** poisoning is practically unknown in the copper-works on Tyneside; nor does occupation in the copper-works appreciably influence any disease that the individual may subsequently suffer from. Occasionally a metallic taste in the mouth and colic are complained of; but I have seen nothing of the vomiting, diarrhœa, and wasting mentioned by some authors. In this I am confirmed by Houlés, who has studied the condition of life in a village full of copper-workers. For the last four hundred years has this industry been carried on therein; sons succeeding their fathers, so that an ancestral integrity has been established. In spite of their long hours of toil in an unhealthy atmosphere, of green lines on their teeth and green hair, the men, though not robust, are healthy, the average age at death being 60. Not only is the metal found in their secretions, but long after death their bones when raked up are green. In copper-workers the gums are discoloured and ulcerated, and the teeth, especially the incisors and canines, are green. On more careful examination, however, it is observed that it is not so much a distinct line of coloration that is present on the gums, as a deposition on the tartar and enamel of the teeth which is easily removed by brushing. Occasionally in old copper-workers the inflammation and ulceration of the gums lead to the exposure of a considerable length of the teeth. The coloration is due to the deposit of particles of copper upon the teeth and their chemical combination with associated matter. Copper has, apparently, none of the serious effects upon work-people that lead and arsenic have; but symptoms generally appear if the copper is combined with zinc as in brass-moulding. Galippe took fairly large doses of copper for one month without any bad effects; and, as dogs to whom the metal was administered did not suffer, it is evident that considerable quantities may be passed into the system without causing much injury. Du Moulin experimented upon himself and family with a similar result. A knowledge of these facts has influenced to a large extent the verdicts of courts of law in regard to the adulteration of food and tinned vegetables by copper; but whilst on the Continent public opinion is disinclined to regard artificially-coloured vegetables as dangerous, in this country several convictions have taken place. So fully convinced is the French Government of the harmlessness of vegetables coloured green by cooking in copper vessels that in 1889 it revoked the law applying thereto.

Copper is therefore regarded by many as not a dangerous metal. The experiments conducted by Laborde, however, clearly indicate that it is not only an irritant poison when given by the stomach, but a cardiac and muscular poison when administered by intravenous injection. It is required of copper, perhaps, more than of other metallic poisons (in contradistinction to those of an animal nature) that the dose must be large; and as vomiting is sure to follow it is by this means at once expelled from the system. In cases where copper has been given in solution and upon an empty stomach absorption has taken place—for the metal has been found post-mortem in the liver, kidneys, lungs, and blood, which on the addition of ammonia give a blue colour indicating the presence of the poison. Admitting that traces of copper may be found in the liver and kidneys of people who during life seemed healthy, and that a kind of tolerance had been established, it must be acknowledged that beyond a certain point the salts of copper are toxic. To produce serious symptoms, however, large doses are required. What constitutes a large dose it is difficult to say, but 40 to 60 grains of copper sulphate repeated in a few hours might prove fatal.

Men who are engaged in making sulphate of copper take little or no harm; there is, practically speaking, no absorption of the drug. A malady known as "brass-founders' ague" is met with amongst those who are engaged in making mouldings of copper, bronze, and brass. Millon as far back as 1847 found that coppersmiths suffered. In 1862 Greenhow drew attention to brass-making as a cause of ill health amongst the workpeople. Previous to both of these writers it is true that Thackrah had written upon the relationship of intermittent fever and brass-founding; but it is to Hogben, to R. M. Simon, and to Arlidge that we are indebted for a full account of the malady. In brass-making, copper and zinc and small quantities of lead, tin and brass-dust are melted together; and it is during the act of pouring this compound from the crucible into moulds that the zinc deflagrates. A dense white cloud of oxide of zinc fills the atmosphere and collects upon the rafters and ceiling of the workshop in the form of a white incrustation. It is notorious that the men, who are called mixers, and who even try to protect themselves by wearing respirators, suffer considerably in ill-ventilated shops from ague and bronchitis. Those who remelt the pig brass, and are called "founders," also suffer from bronchitis and asthma, but less severely from ague; although from the molten compounds clouds of zinc are given off. The metal after being polished is sent to the "dippers," who work in an open shed: they dip the brass first into a weak and then into a stronger solution of sulphuric acid and soda; afterwards it is placed into pure sulphuric acid, and washed. These men do not suffer from ague or intestinal troubles; but it is admitted that the work is dangerous to health from the great bronchial irritation caused by the acid fumes. According to Simon it would appear that those who are engaged regularly at brass-making do not suffer from ague; it affects rather those who are new to the work, or who have absented themselves from it for a time. Thus a degree of tolerance seems to be established towards it. In a new-comer the exposure of a few hours to the molten metals suffices to produce the ague. The individual soon becomes languid, depressed and cold; he is pale and collapsed, his face is covered with a cold perspiration, he shivers, his teeth chatter, headache, nausea and vomiting follow, and after this there usually comes relief. The hot and sweating stages of ague, if present, are scarcely recognisable. In no manner, therefore, can this attack due to metallic poisoning be compared to malarial ague. The teeth of the men, in spite of the use of the tooth-brush, are always discoloured green. The white hair of the work-people is frequently coloured green. Although this so-called ague is of common occurrence, the men seldom go to hospital on account of it. They know how to treat themselves. Some of the men who are engaged in the dusty part of the factory ultimately succumb to chronic bronchitis and fibroid phthisis. The records of their own Union Society show that they are a short-lived body of men. Nervous disorders also occur with considerable frequency amongst them. Suckling and Schloehow allude to the frequency of ataxia, and Hogben speaks of progressive paresis of the legs, tremor, and muscular wasting as also occurring in them. Brass-workers suffer from gastro-intestinal disturbance, nausea, vomiting, a metallic taste in the mouth, colic, constipation or diarrhœa, headache, and muscular pains—a series of symptoms which I have also observed in men who work in boot and shoe factories, and who whilst engaged in soling boots hold brass nails in their mouths. These men become pale, and are frequently the subjects of colic and gastro-intestinal trouble.

It is difficult to say how far the symptoms met with amongst brass-workers are due to copper or zinc. Dr. Stevenson of Guy's Hospital maintains that it is impossible to distinguish between zinc and copper poisoning. Greenhow believed that the symptoms were due to zinc, Hogben to copper; whilst Simon regards the ague symptoms as due to the admixture of the metals, and the more chronic complaints as due to the copper. The workmen themselves have found out that milk is the remedy during the attack of ague; but industrial prophylaxis—such as complete ventilation, the wearing of respirators, and personal cleanliness—is imperative.

For the detection of copper the text-books on toxicology may be consulted. It is sufficient here to mention that with fluids containing copper—(i.) ammonia gives a blue colour; (ii.) ferrocyanide of potassium a brown-red colour or precipitate; (iii.) the addition of tartrate of soda and sodium hydrate, and boiling with a few grains of grape sugar, give a red precipitate of oxide of copper; and (iv.) a needle, or the clean wire of a galvanic battery, if immersed in the suspected fluid soon becomes coated with a red metallic film.

ZINC.—Accidents occasionally follow the use of zinc salts, especially of the chloride and sulphate. For years past experts have been in search of a pigment as a substitute for the white carbonate of lead so freely used in painting; and both the sulphide and oxide of zinc have been recommended. This subject was carefully inquired into by the White Lead Commission; and whilst it is admitted that for internal decorative purposes oxide of zinc gives on the whole satisfactory results, it has not the covering power, the permanence, nor the resistance of white lead to extremes of temperature and inclement weather. Zinc white (oxide) is used in calico printing, in the decoloration of glass, and in the manufacture of artificial meerschaum pipes. As zinc is largely present in vessels in which food is sometimes cooked, contamination of the food may occur; for the metal on being exposed to the air becomes coated with a film of oxide of zinc which, though insoluble in water, becomes readily soluble if a trace of chloride of sodium be present. The presence of chlorides generally favours the solvent action of water upon zinc, whilst carbonate of lime diminishes it. Milk may thus become readily contaminated. Milk contained in zinc vessels does not become sour, probably because the zinc oxide combines with the lactic acid forming the very sparingly soluble lactate; thus is withdrawn from the milk the lactic acid upon which its souring depends. According to Harnack zinc salts produce paralysis of the cardiac and voluntary muscles. The oxide of the metal may cause death in rabbits in the proportion of 0·08 gramme to 0·04 kilo of the animal. In my own experiments zinc oxide was administered to animals over a very long period, and in considerable doses; but when the drug was perfectly pure none of the rapidly fatal results occurred which Falck and others described. One of the reasons why zinc oxide has been so strongly recommended to house painters is its harmlessness compared to lead carbonate. I am not prepared to say that zinc white is absolutely innocuous; but rabbits take it by the mouth for many months without seeming to suffer much discomfort; and in the mixing department of large colour works men who breathe the dust and whose clothes are covered with the white powder do not, as a rule, suffer any inconvenience. It may seem to cause headache, nausea, vomiting and cramp-like pains in the limbs; but as zinc oxide is frequently impure, containing small quantities of lead and arsenic, these symptoms are more probably due to the adulteration than to the metallic compound itself. Spelter workers in this country—that is, men who smelt zinc ore —occasionally suffer from plumbism, owing to the small quantities of lead which the ore contains; but there are few or no bad effects from the pure zinc fumes. Zinc smelters, according to Schlockow, rarely live beyond the age of forty-five years. They frequently die from catarrh of the bronchial or pulmonary mucous membrane accompanied by peculiar nervous symptoms, beginning with burning sensations and heightened reflex excitability in the legs, and followed by signs of myelitis.

Death from chronic zinc poisoning, or from the sulphate, is extremely rare. However irritant a poison the latter may be, it is such a strong emetic that by means of the vomiting which it causes its elimination is at once accomplished. Sulphate of zinc, to the extent of one ounce, has been taken by mistake for Epsom salts. The patient suffered from violent vomiting and purging, severe cramps in the legs, and great prostration; but he recovered. The salt has, however, caused death, the symptoms being vomiting, purging, collapse, and death in thirty hours. Subsequently zinc was found in the stomach, liver, and spleen. Penfold relates the case of a girl who died 3½ hours after taking sulphate of zinc to produce abortion.

Zinc chloride is a stronger poison, and is capable of killing by its primary and secondary effects. It has a powerful affinity for water, and dehydrates the tissues with which it is brought into contact; to this peculiar influence its caustic action is due. Burnett's disinfectant fluid, which contains large quantities of zinc chloride, has been a frequent cause of poisoning in this country. Death has followed the repeated external application of Canquoin's paste—a mixture of zinc chloride, flour, and water—as a cure for cancer; the symptoms observed during life being those met with in zinc poisoning, namely, a burning pain in the lips, tongue, and throat, excessive salivation, bloody vomit, diarrhœa, collapse, and death within a few hours. When death has not rapidly followed, a peculiar group of symptoms has arisen; for example, a perverted sense of taste and smell, aphonia, spasms of the voluntary muscles, great fatigue, and impaired vision. A dose of 6 grains of zinc chloride has caused death, while as large a quantity as 200 grains has been recovered from. Zinc chloride may be present in canned vegetables, owing to zinc dissolved in hydrochloric acid having been used for soldering the tin.

When sulphate of zinc has proved fatal there have been evidences of inflammation of the stomach and bowels accompanied by a peculiar tripe-like wrinkling of the mucous membrane; whilst the surface presented a uniform dirty gray colour. In death from chloride of zinc the lining membrane of the mouth and throat is white and opaque, the stomach is hard and leathery, congested or ulcerated. When the fatal issue has been postponed for a time cicatricial contraction of the œsophagus and stomach has occurred.

The treatment of the acute poisonous symptoms due to zinc salts consists in the administration of eggs and milk, tannin or green tea; and in the allaying of gastric irritability. The more chronic symptoms must be treated on general principles as they arise.

For the detection of zinc in organic liquids or solids the elaborate methods described in text-books on chemistry and toxicology must be used. Even in cases where the vomiting has been profuse and the drug is supposed to have been thus expelled from the system, the muscles and bones should be carefully examined, as in them traces of zinc are generally to be found. The most satisfactory test for the identification of zinc consists in the production of Rinman's green. It is based upon the production of the sulphide of zinc, and is best accomplished by saturating the neutral or feebly acid suspected liquid with sulphuretted hydrogen. "The supposed sulphide is dissolved off the filter with hot nitric acid, a drop or more (according to the quantity of the original precipitate) of a solution of cobalt nitrate added, the solution precipitated with carbonate of soda and boiled, to expel all carbonic anhydride; the precipitate is then collected on a filter, washed, dried, and ignited in a platinum dish. If zinc be present in so small a proportion as 1·100,000 part, the mass will be permanently green" (5).

ANTIMONY.—In this country there are very few antimony works; of these one of the largest is on Tyneside. Here large quantities of sulphide of antimony, the raw material that comes from the mines of Japan, are smelted along with iron filings; the result being sulphide of iron and pure antimony. The men who smelt the ore suffer no bad effects, practically speaking, from the fumes of the metal. The workmen are not brought into such close contact with the molten metal as in the smelting of some other ores; besides, the industry is carried on in well-ventilated shops. The only trouble, and it is more of the nature of an inconvenience, that is felt by the men is that as their work is hot and they perspire freely, the skin is extremely liable to become the seat of a herpetic eruption, at first vesicular, subsequently pustular, and excessively itchy. This eruption, which is called by the workmen the "pox," occurs where the skin perspires most freely—behind the neck and along the upper part of the abdomen. Eulenburg states that workmen who have long been exposed to the fumes of the oxide of antimony suffer from vesical and urethral pains, and atrophy of the testicles leading to impotence. Several of these men whom I have examined were pale; but only one or two of them had suffered from colic and gastro-intestinal disturbance, and this very slightly. Antimony smelting does not, therefore, appear in itself to be a dangerous industry. The pure metal is employed for making printers' type—in the finishing of which, however, the dust is inhaled which is said to cause colic exactly resembling that of plumbism. Probably this is due rather to lead, which is present in type-metal, than to the antimony itself.

Of the antimonial salts, tartar emetic—a tartrate of potass and antimony—is the most important. Two grains of this have proved fatal to an adult, and two-thirds of a grain to a child. Horses and cattle exhibit a wonderful tolerance of the drug: they can take from 60 to 90 grains three times a day without much inconvenience. Whether tartar emetic be administered to man or the lower animals, by the mouth or subcutaneously, the effect is the same—vomiting takes place, and the heart's action, which is at first quickened, becomes slower and paralysed, probably from the direct action of the drug upon the heart; the organ ceases to beat in diastole.

When given in small doses to animals, and for a long time, diarrhœa, great hebetude, loss of appetite and emaciation have been observed; pregnant animals have miscarried. Death has been preceded by convulsions, and in the mouth of several of the animals small ulcers have been observed. In man the symptoms resemble those produced by arsenic. If the dose of tartar emetic has been large, vomiting may not occur, or it may be accomplished with difficulty: there may be violent pains in the abdomen and purging, with rigidity of the muscles of the abdomen and arms, followed by profuse perspiration, continuing for several days. Applied to the skin in the form of ointment it may give rise to a pustular eruption and be followed by vomiting and purging.

If very small doses be given for a long time a metallic taste in the mouth is complained of, also frequent vomiting—the vomit being sometimes bloody—great faintness and bodily weakness, pains in the abdomen and diarrhœa. Should the case advance to a fatal termination death is often preceded by suppression of urine, a marked fall of the temperature, cyanosis of face, delirium and convulsions. Frequently there is a pustular eruption on the skin. The Palmer and Pritchard trials demonstrated that even medical men might mistake the symptoms of chronic antimony poisoning for natural disease—the symptoms being nausea, vomiting, chronic diarrhœa alternating with constipation, a small, frequent pulse, loss of voice, great muscular weakness, coldness of the skin, and clammy perspiration. In other cases flushing of the face with mental excitement, suggestive of mild alcoholic intoxication, has been observed.

The post-mortem appearances met with in poisoning by tartar emetic are inflammation of the stomach and intestines, with small ulcers and pustules; or larger ulcers that are sloughing. The solitary glands of the intestine may be enlarged and yellow, whilst the liver, kidneys, and heart show signs of fatty degeneration.

Like the other metallic poisons antimony is eliminated by the urine; hence in cases of suspected antimonial poisoning the urine of two or three days should be collected, concentrated by evaporation, and acidified with hydrochloric acid. This fluid is subsequently transferred to a platinum dish in which is placed a slip of zinc or tinfoil. By means of ammonium sulphide the antimony is dissolved out as the yellow sulphide. For more complete analyses Reinsch's or Marsh's test may be employed.

Towards antimony people exhibit a peculiar idiosyncrasy. Some are easily affected by the minutest dose, others are extremely tolerant of it. It is well to remember that, as tartar emetic rapidly leaves the body by vomiting and purging, only the smallest trace of antimony may be found in the body after death; a fact of which lawyers engaged for the defence in criminal cases are apt to make the most.

Treatment.—As poisoning by antimony is generally due to tartar emetic it is more than probable that the patient will have vomited freely: if not, the stomach-pump must be employed. Once the stomach is thoroughly washed out there should be passed into it some strong infusion of tea or tannin. Should vomiting not have occurred, or the stomach-pump be inaccessible, a hypodermic injection of apomorphine, $\frac{1}{10}$th of a grain repeated every ten minutes, or $\frac{1}{4}$th of a grain at a single administration, is called for. Subsequently demulcent drinks are of great service. As there is a tendency for considerable bodily depression and a fall of the temperature to take place, the heat of the body must be maintained by the application of hot bottles and warm blankets, and the administration of stimulants by the rectum. Should signs of cardiac failure be present, the application of the interrupted galvanic current to the chest must be resorted to.

There is a form of antimonial poisoning in which, according to Husemann, neither vomiting nor purging occurs; where the symptoms are those of intense prostration as indicated by a cold clammy sweat, embarrassed and infrequent respiration, feeble, slow and intermittent pulse; and in which delirium, tremors or convulsions followed by unconsciousness appear, or the patient, after protracted vomiting and purging, dies from sheer exhaustion. For such cases stimulants and subcutaneous injections of ether are necessary.

Industrial poisoning from antimony hardly ever occurs. Working in well-ventilated "shops," attention to the state of the bowels, regular living and temperance, and personal cleanliness on the part of those engaged in smelting the antimony ore, are desirable; and for the skin eruption or "pox" as it is called—which is due to excessive perspiration—sponging with a solution of bicarbonate or biborate of soda, or of boracic acid and bismuth, is generally sufficient to give relief. Abstention from work might be necessary.

CARBOLIC ACID.—Carbolic acid is obtained from phenic acid or phenylic alcohol, a product of coal-tar distillation. It is used in the manufacture of dyes and salicylic acid. Although known in 1834 it was not until 1863 that Lister introduced it into surgery, since which time it has become widely used as a disinfectant. Being thus so easily within the reach of the public, carbolic acid poisoning has become extremely common, particularly among women. In England it stands sixth on the list of all fatal cases of poisoning. The history of carbolic acid poisoning is comprised within our own times. From the first recorded case of accidental poisoning in 1864, and of two suicides in 1869, there has been a rapid increase in the annual number of deaths from this cause. In the five years ending 1870, suicide by carbolic acid first appears in the Registrar-General's Reports to the extent of 1·0 per cent of all suicides by poison. In the quinquennium ending 1875, 128 deaths are reported, nearly 25 per annum; 42 of these are suicidal, 23 females and 19 males. It was in this period that the Public Health Acts were passed (1872-1875), and, as a consequence of the general interest aroused in sanitation, carbolic acid, then regarded as a reliable disinfectant, came within easy reach of the people, and began to serve as a means of self-destruction. An increase of 135 per cent occurs in the number of deaths by this poison during the five years ending 1880, the deaths being 181, of which 81 (53 females and 28 males) were suicidal; that is, 7·8 per cent of the suicides from all poisons. In the quinquennium ending 1885, 302 deaths from carbolic acid poisoning are registered, of which 191 (99 females and 92 males) were self-caused; that is, 15·6 per cent of all suicidal poisonings. For the five years ending 1890, 342 deaths are recorded, of which 215 were suicidal; an average of 43 per annum, and 15·4 per cent of all suicides by poison. During the four years ending 1894 the number of deaths from carbolic acid poisoning had still increased: 549 deaths having been reported, of which 420 or 76·5 per cent are suicidal, equal to 105 annually. The history of carbolic acid poisoning, as detailed by Harris, is a gloomy record, for whilst it formed 5·8 per cent of all suicidal poisoning in 1871-75 period, it has lately caused 28 per cent. In the period 1861-65 the suicides by carbolic acid were 0·00 per cent of all suicides from poisons; in 1866-70, 1 per cent; in 1871-75, 5·82 per cent; in 1876-80, 7·93 per cent; in 1881-85, 15·37 per cent; in 1886-90, 15·49 per cent; and in 1890-94 (four years), 28·01 per cent.

Carbolic acid causes severe symptoms whether swallowed by the mouth, breathed as vapour, administered in enema, applied to the broken skin, or taken in large doses in the form of carbolate of soda. Less than half an ounce of pure carbolic acid has proved fatal. The dark carbolic acid of commerce owes its colour to such impurities as cresol and cresylic acid —substances which render it stronger as a germicide, but only one-fourth as poisonous to the higher animals. When a strong solution of carbolic acid is applied to the skin it causes a peculiar numbness, followed later by irritation, and usually by a pustular eruption or desquamation of the skin, which, white at first, afterwards becomes brown. Messrs. Clement Lucas and Lane have reported two cases in which coma and other serious symptoms arose from the application of a 1 in 20 solution to the skin; and similar effects have followed the washing out of empyemas and large abscess cavities. After a few days' successive washing out of the pleural cavity symptoms of poisoning have compelled suspension of the treatment. The application of strong carbolic acid to the interior of the uterus and cervix uteri in one of my own patients caused extremely unpleasant symptoms, accompanied by a rise of temperature; and similar but more severe symptoms were observed in obstetric practice by Kuster, on washing out the uterus with a 5 per cent solution of carbolic acid. The patient became livid, clonic convulsions supervened with temporary loss of consciousness, and death followed on the ninth day; the uterus and vagina being the seat of an intense diphtheritic inflammation (46). It has been conclusively demonstrated that women who have lost large quantities of blood, or who are the subjects of septic fever, are peculiarly sensitive to the influence of carbolic acid: so likewise are children. The effects of the acid upon animals are similar to those observed in man. Crude carbolic acid applied accidentally over a large part of the skin has caused extensive burns, rapid unconsciousness, and death in a few minutes.

If a large dose has been swallowed there is complaint of burning in the mouth and throat; the patient feels faint; the face becomes pale and covered with clammy perspiration; unconsciousness and perhaps convulsions gradually supervene; the breathing becomes shallow and laboured, and death comes soon after from respiratory failure, the heart beating for a few minutes after breathing has ceased. Resuscitation in some cases may be yet effected by artificial respiration. The vomit is frequently bloody and smells strongly of the poison. The lips are dry and frizzled; the tongue is white or brownish; the patient cannot allow the epigastrium to be pressed on account of pain. The temperature tends to fall at first, but it may rise within the next few days and the patient may complain of an intolerable thirst. In cases of carbolic acid poisoning a peculiar colour of the urine is an almost constant phenomenon: it varies in tint from light yellow or a dirty green to a dark brown or blackish green on exposure, and may emit a sweet odour. It may or may not contain albumin. In any case where such a discoloured urine has been passed by a patient who is the subject of coma or convulsions, the diagnosis of carbolic acid poisoning may be made with certainty. According to Baumann the darkened colour of the urine is due to the fact that when carbolic acid is taken internally it is eliminated as phenyl sulphuric acid or, more strictly speaking, as potassic phenyl sulphate; and from this hydrochinon and pyrocatechin are formed, which on exposure to the air become dark brown by oxidation. According to Prof. Halliburton, pyrocatechin, like sugar, has the power of reducing alkaline solutions of copper salts. Thudichum states that after the ingestion of carbolic acid a blue pigment is found in the urine. The blood of animals poisoned by this acid presents nothing abnormal; so that whilst the colour of the urine suggests the presence of altered blood-colouring matter or hæmatin, chemical facts do not support this supposition, for the urine clears up on heating after adding an acid. Dr. Stevenson of Guy's Hospital states that the urine does not contain more than the normal proportion of iron; and Brieger maintains that when carbolic acid is taken internally it unites with sulphuric acid, and various coloured oxidation products are formed, some of which are very poisonous. Chemical opinion, therefore, leans to the view that the acid when swallowed enters into sulphuric acid relationships, and that the tendency is for the ordinary sulphates to disappear from the urine. Hoppe-Seyler, Nencki, and Brieger believe that carbolic acid is a constituent of normal urine, and that it is present also in the fæces, its source being the tyrosin obtained from proteids acted upon during pancreatic digestion; thus man may normally develop a disinfectant within his own intestine (105).

As carbolic acid coagulates albumin the absorption of the drug has been questioned; yet there is considerable evidence to show that it is absorbed; it is eliminated as such in the urine, which also contains numerous oxidation products derived from it. We do not exactly know the form in which it circulates in the blood, but it is probably as an alkaline carbolate. It is retained for a short time only within the system, being rapidly thrown out in the excretions.

In animals killed by carbolic acid the post-mortem appearances have occasionally been simply an intense injection of the alimentary and bronchial mucous membranes, and congestion of the lungs. The cells of the liver and kidneys undergo fatty degeneration—this change being most pronounced in the renal epithelia. In man similar appearances have been found after death. The mucous membrane of the mouth, œsophagus, and stomach may present numerous white spots, with occasionally a dark centre and an inflammatory border, due to the local action of the poison. The liver, kidneys, and spleen may be congested and filled with dark liquid blood. In one of my male patients who died on the 8th day after swallowing an ounce of carbolic acid the vomit on microscopical examination showed numerous large flattened epithelial cells, extremely fatty, which had evidently come from the mouth and œsophagus; and similarly in the urine, in addition to masses of débris, were many round cells, the seat of marked fatty degeneration. The urine, although albuminous, contained a normal percentage of urea. On the 5th day several sloughs of gastro-intestinal mucous membrane two inches in length and of a yellowish brown colour were passed by the anus without any bleeding. The day before death the heart rapidly dilated, a mitral systolic murmur appeared, and the sounds became extremely feeble.

In cases of acute carbolic acid poisoning there is generally a distinct odour of it in the breath; this, with the presence of white patches on the lips and mucous membrane of the mouth, and, later, the altered colour of the urine, are sufficient to point to the real nature of the illness. As in some cases neither discoloration, whitening, nor congestion of the lips and buccal mucous membrane are observable, the medical attendant may be thrown off his guard unless he has a history of the case to guide him, or a phial is found containing poison. The use of the stomach-pump and washing out are immediately called for. Emetics are of little service, for, owing to the anæsthetic state of the stomach, they fail to obtain a response. Whilst the administration of alkalies in excess is useful, Baumann and Hueter have shown that the antidote to carbolic acid poisoning is a soluble sulphate; for during this form of poisoning sulphates disappear from the urine, and if a soluble sulphate is supplied it enters into combination with the acid, forming the less harmful sulpho-carbolate which is rapidly eliminated. Other writers, notably Sonnenburg and Cerna, have confirmed the value of alkaline sulphates in the treatment of acute carbolic acid poisoning. The former found that the dark colour of the urine and other symptoms rapidly disappeared under the administration of sodium sulphate; and Cerna in his experiments upon animals had equally good results from the administration of magnesium sulphate. But these alkaline sulphates, to be efficacious, must be exhibited freely. Schobert recommended saccharate of lime as an antidote to phenol poisoning, so long as the poison is still in the stomach; after it has passed into the intestine he gives sodium sulphate. The saccharate of lime he prepares thus:—

Fresh quicklime	15 parts.
Sugar	25 "
Water	1000 "

and of this mixture fairly large quantities may be administered. In one of my own cases, where consciousness was long in returning, we transfused the patient with saline solution, containing sulphates, in the hope of forming harmless compounds and of washing out the poison by the kidneys. Two days afterwards the urine was quite clear; it had lost the colour so frequently observed in these cases. Thirst may be relieved by lime-water and milk. On account of the pain in the mouth and throat nutrient enemas may be necessary.

Since the introduction of the intestinal antiseptic treatment for the various forms of auto-intoxication due to the absorption of poisons elaborated within the alimentary canal, carbolic acid pure, or in combination with soda as sulpho-carbolate, has been freely prescribed. Of the beneficial effects of this line of treatment there is no doubt. The drugs should be given with a certain amount of care, and not for too protracted a period; as the urine may become discoloured and the patients complain of much malaise. In the early days of antiseptic surgery, when the carbolic spray was more employed than now, for instance in cases of ovariotomy, it was no uncommon thing for those assisting at the operation to suffer from it as well as the patient; their complaint being headache, a general feeling of malaise, altered sensibility of the skin, and occasionally vomiting.

The urine from a case of carbolic acid poisoning may be normal. Much more frequently it is yellow when passed; gradually it becomes dark olive, and finally dark brown or blackish green. If treated with nitric acid and then with liquor potassæ, it becomes after concentration blood red in colour, and changes through pea green to violet; a fact of some importance, for on the simple addition of carbolic acid to urine the mixture does not respond to this test. Sometimes the fæces have the odour of phenol and are dark olive green in colour.

BISULPHIDE OF CARBON.—Owing to the solvent influence of bisulphide of carbon upon various resins, such as caoutchouc, or gutta percha, this substance is largely employed in certain industries. It is a colourless, volatile fluid, with a most penetrating and repulsive odour, and is most destructive to all noxious insect life. Delpech first drew attention to poisoning by carbon bisulphide; and to what he wrote in 1863 in *Les Annales d'Hygiène Publique*, p. 65, little has since been added. His experience was gained in the india-rubber works in Paris, which at that time were very badly ventilated. Carbon bisulphide is used to soften india-rubber so as to allow of its penetration by sulphur in the carrying out of what is known as vulcanisation. During this process the vapour of the bisulphide is inhaled. As a result intoxication follows, and of this there are two stages—(i.) excitation, and (ii.) collapse—an order which resembles that of the intoxication of anæsthetics or alcohol. The illness may be sudden or delayed; the symptoms are headache, cramp-like pains, epileptiform seizures, muscular tremors, imperfect vision or amaurosis, and faintness. There may be great mental excitement or depression. Women suffer from menorrhagia, and if pregnant they miscarry. In the early stages of the intoxication there is sexual excitement; but in chronic poisoning this abates, for in men atrophy of the testes ensues, and in women sterility. The symptoms occasionally resemble those of general paralysis, acute mania, or alcoholism. Dr. Ross of Manchester observed paralysis analogous to that met with in plumbism; a condition regarded by him as due to peripheral neuritis, marked by a gait not unlike that of locomotor ataxia and accompanied by absence of the knee-jerk. In some respects the neuritis resembled that of alcoholic poisoning; but the muscles were not hyperæsthetic, and loss of colour-vision and amblyopia were present, due, as Mr. Simeon Snell believes, to optic neuritis. Schweinitz maintains that it is an intoxication-amblyopia similar to that caused by tobacco. One-third of the patients regain their sight. Ross reports the case of a worker in an india-rubber factory, who complained of the smell of the bisulphide of carbon always being with him, in his food, and in his home; and on leaving work in the evening he would walk like a drunken man and talk a good deal of nonsense. In the following morning he would be miserable and feel wretched. He was glad to get back to work, as inhalation of the vapour seemed to act as a stimulant and bring relief. The muscles of his hands, forearms and legs wasted; his grasp became feeble, and numbness and tingling of the hands and feet were complained of. In walking his gait was that of a high-stepping horse, due to paralysis of the muscles that produce dorsal flexion of the foot. There was double "foot-drop": the knee-jerks and the reflexes of the soles were absent, but the other cutaneous reflexes were normal.

In my own experiments upon animals bisulphide of carbon was found to be a very deadly poison. It is an anæsthetic, even more rapid in its operation than chloroform, and as profound in its effects. Inhalation of the vapour for a short time by a rabbit was followed by signs of intense excitement. When placed on its feet the animal seemed to be intoxicated, kept swaying from side to side, and then, as if seized by some sudden impulse, bounded forward heedless of objects in its path. When the inhalation was pushed further, not only was there profound sleep with deep stertor, but on regaining consciousness the hind limbs of the animal were paralysed; and so they remained for more than an hour. When rabbits were exposed for a long time to the vapour of bisulphide of carbon, which entered their hutches from an adjoining chamber, they quickly succumbed; one in three days and another in twenty-one. They lost flesh, became tremulous, were easily fatigued, became paralysed in their hind limbs, and died convulsed. All through the period of inhaling the bisulphide the renal function was excessive; and the urine at death, whilst free from albumin and almost completely awanting in urea, contained a very large quantity of sugar. The large cells in the motor areas of the brain were found after death, on staining by Golgi's method, to have their axis cylinders distorted and varicose; and the cytoplasm of the cell took on staining unequally. Sections of brain stained by Nissl's method, however, did not exhibit this peculiar change to R. A. Bolam or myself. Dogs were readily anæsthetised by carbon bisulphide. It seemed to be a pretty safe anæsthetic, but apart from its extremely disagreeable odour, it produced too much muscular jactitation to be regarded as a desirable substitute for chloroform. The red blood cells, whether in dogs or rabbits, did not exhibit any sign of disintegration; and, contrary to the statement of other writers, the blood on spectroscopic examination showed no trace of methæmoglobin, but simply of oxyhæmoglobin.

I have described the results of these experiments upon animals because they correspond so closely to those exhibited by man. In my visits to the various india-rubber factories of the country, I have become sensible of the enormous amount of suffering which vulcanisation of rubber goods by the "wet" method inflicts upon the work-people. I saw several men who for months had been paralysed in their arms and legs. Many girls had suffered from incomplete loss of power in their hands and legs, headache, vomiting, and extreme drowsiness: so that on reaching home on an evening they would fall sound asleep on sitting down for a few minutes. Many felt so dizzy, and so frequently lost control of their legs, that they staggered as if intoxicated, and occasionally fell on their way home from the factory. Their sleep at night was heavy and unrefreshing. When the weather is hot and close the work-people suffer most. In one factory brought under my notice three cases of acute mania have occurred; in each case the sufferer was driven by some sudden impulse to throw himself from the top story of the building. Peterson of New York reports a similar result, namely, violent destructive mania. Charcot has drawn attention to the hysterical character of some of the symptoms; for example, hemianæsthesia with hyperæsthetic patches. The acute stage, however, must be simply regarded as an intoxication.

In an acute case of poisoning, where two ounces of the bisulphide were swallowed without a fatal result, there were pallor of the face, dilated pupils, frequent small pulse, low temperature, and an odour of the poison which was detected in the breath. By passing the expired air through an alcoholic solution of triethyl-phosphin it produced a red colour. The symptoms resemble those caused by alcohol, and especially those of delirium tremens. Bisulphide of carbon is a strong toxic agent capable, like lead and arsenic, of producing paralysis from polyneuritis. Faradaic irritability of the muscles is generally diminished, and frequently the sense of taste is lost.

The treatment consists in the removal of the patient from his work, placing him in good hygienic surroundings, and allaying all excitement by means of rest. Good food, massage and galvanism, with tonics as aids to digestion, are required when nerve symptoms are present.

NITRO- AND DINITRO-BENZOLE AND ANILINE POISONING.—Within the last few years, owing to the impetus given to the manufacture of aniline dyes, numerous cases of poisoning by nitro- and dinitro-benzole have been reported in this country, in Germany, and in the United States. Nitro-benzole is largely employed in perfumery, and is known as the essence of mirbane or artificial almond scent. In cheap confectionery it is used as a substitute for the essential oil of bitter almonds. Its principal use, however, is in the manufacture of aniline, and in the preparation of the explosives known as roburite and sicareit; in the manufacture of these substances the vapour of nitro-benzole is inhaled, or particles of its dust become deposited upon the skin. Benzole is a coal-tar product, and when treated at a moderate temperature with nitric and sulphuric acid it becomes nitro-benzole; treated further at a higher temperature it becomes dinitro-benzole. Some of the injurious consequences of dinitro-benzole are attributed to the presence of impurities; but it is generally admitted that dinitro-benzole itself acts as a poison, whether it be ingested, absorbed by the skin, or inhaled by the lung in the form of vapour or dust. The recent contributors to the literature of nitro-benzole poisoning are Dr. Prosser White of Wigan, Dr. Reynolds (82), and Mr. Simeon Snell.

Nitro-benzole poisoning is purely an industrial accident. The men who breathe the vapour, and who are said to suffer more than those who have swallowed it, are sometimes suddenly seized with alarming symptoms. They become extremely sleepy, complain of severe throbbing headache, and occasionally vomit. To these symptoms may be added dyspnœa, dilated pupils, cardiac irregularity, loss of voluntary power, ataxia and extreme cyanosis. The urine is reddish brown in colour, and from it and the breath the odour of bitter almonds is exhaled. The patient rapidly passes into a state of coma with symptoms of apoplexy, death being preceded by Cheyne-Stokes respiration. The skin and tongue are discoloured dark blue, probably from the presence of aniline. Such are the symptoms of acute cases of nitro-benzole poisoning. The blood is of a dark chocolate colour, and has lost its power of absorbing oxygen. According to Starkow and Filehne it gives a spectrum similar to that given by acid hæmatin; namely, one absorption band in the yellow between C and D, two between the lines D and E, and a further band to the right. Methæmoglobin gives a similar spectrum. It is interesting to know that blood mixed with dinitro-benzole outside the body does not give these bands except after long exposure to the air and heating.

Death from nitro-benzole poisoning has generally been preceded by coma, although convulsions have been observed. After death the skin is found pale or blue; the brain is congested; the blood all through the body is thick, dark, and fluid; the cavities of the heart are dilated, and the lungs dark or very pale. From the stomach and other internal organs a strong smell of bitter almonds is emitted.

Fifteen drops of nitro-benzole may prove fatal. The rapidity with which symptoms appear after swallowing the poison is greatly determined by the state of the stomach. When large quantities of vapour have been inhaled the symptoms may appear within a very short time—from twenty-five minutes to two hours; and death may follow within a few days. If injected into the veins, the poison, according to Filehne, is almost as rapidly fatal as prussic acid.

In acute poisoning the diagnosis is made from the history, the symptoms, the physical signs, and the peculiar odour of bitter almonds. The principal difference between nitro-benzole and prussic acid poisoning is that the symptoms of the latter are immediately manifested; whilst in nitro-benzole poisoning they are latent or delayed for hours. Should the poison have gained access by the stomach this organ should be washed out. Sinapisms should be applied to the chest and friction made upon the limbs. Stimulants, such as ammonia, or injections of camphor, are called for. Artificial respiration and the application of the faradaic current, may be necessary to rouse up the patient.

In the less acute cases so fully described by Prosser White the skin is generally of a dirty yellow colour. There is great languor and loss of weight, and the tendency to sleep is very marked. Men who are thus suffering find it almost impossible to keep awake; yet although they sleep soundly at night, they awake unrefreshed in the morning, generally with severe headache, occasionally with giddiness, and with almost complete loss of appetite for breakfast. The temperature is often one degree above the normal, the breathing is quickened, precordial and muscular pains and feebleness are complained of. Fatigue is easily induced. The movements become ataxic, and are aggravated on closing the eyes. Tingling and a sense of numbness are complained of in the fingers, hands, and feet; there is hyperæsthesia, which in certain areas is extremely marked, or there is partial hemianæsthesia. The reflexes may be increased or diminished, usually the latter. The muscles react to faradaism, but they vary in their sensitiveness to the current. One of the most characteristic signs of nitro-benzole poisoning is a dark maroon colour of the urine. Although like port wine in colour it contains no blood. If the urine, which is acid, be gently warmed, the odour of bitter almonds is readily obtained. The deep colour of the urine depends upon the presence of aniline, nitro-aniline, or some coloured product due to the reduction of the nitro-benzole. The bile pigments in the urine are increased. Patients thus ill usually throw off an excess of urea. The blood is generally of a chocolate colour, and is poor in red corpuscles, which are diminished in size and deficient in hæmoglobin. The blood contains an excess of carbon dioxide, which may partly explain the dyspnœa and cyanosis. In poisoning by aniline cyanosis occurs, a circumstance which, with other facts, favours the presumption that nitro-benzole is changed by oxidation and reduction in the body into aniline or possibly hydrocyanic acid, and dinitro-benzole into one or more of the phenyl-diamine series, which are more toxic, and that the symptoms of poisoning are due to aniline. We are still ignorant of the nature of the chemical changes which nitro-benzole undergoes in the body; but it would appear that it may form picric acid in the blood, to which substance the yellow colour of the skin and of the mucous membrane of the intestinal tract has been ascribed by Eulenberg. The substances belonging to this group act as poisons to the medulla oblongata and other portions of the central nervous system, producing peripheral neuritis, and symptoms similar to those of locomotor ataxia and disseminated sclerosis. According to Brunton they have a direct influence upon muscle-fibre itself. Nitro-benzole rapidly affects the brain, judging from the lethargy and drowsiness so frequently exhibited, and coma. Recovery is possible even when consciousness has been lost for days; but the greatest care must be exercised, as, some time after recovery had apparently taken place, sudden death has occurred in lifting the patient. To Simeon Snell we are indebted for an account of the amblyopia in dinitro-benzole poisoning. There is often failure of sight to a considerable degree, which is generally equal in both eyes; there is concentric contraction of the visual field with, in many cases, a central colour scotoma, enlargement of the retinal veins, slight blurring of the disc, and pallor of its surface. Snell believes that the enlargement of the retinal veins is due to vaso-motor paralysis.

It is absolutely necessary in factories where nitro-benzole is manufactured that only men with robust constitution should be employed; that the rooms they work in should be well ventilated, and the temperature not high (for Prosser White has shown that a low temperature is always accompanied by a decrease in the sick-rate); that respirators and special clothing should be worn; personal cleanliness observed; the use of alcohol forbidden, and above all that the hours of labour should not be long. From the rapid emaciation of the men, and the excessive elimination of urea, it would appear as if the metabolism of the tissues was extremely active; hence the necessity that workers in nitro-benzole should be well fed upon animal food, and that employers should provide them with milk when in the factory.

There is no known antidote to these poisons. If swallowed, the stomach-pump should be used and this viscus thoroughly washed out. Oils, fats and alcohol are contra-indicated. Faradaism and sinapisms may be applied as mentioned in an earlier paragraph. Special rules have been framed for the protection of the health of workers in nitro-benzole factories by Dr. Dupré and Captain Hamilton Smith (*Report H.M.'s Inspect. Factories* 1894).

Aniline.—Aniline, of which mention has frequently been made in this chapter, is obtained from coal-tar oil or naphtha. It is the first substance formed during the process of manufacture of benzole, or benzene. This is subsequently converted into nitro-benzole, from which aniline oil is obtained, the source of all magenta dyes. Aniline is a narcotic poison, acting upon the central nervous system, causing insensibility, convulsions, and motor paralysis. Workmen in the factories complain of vertigo, stupor, muscular spasms, deranged sensibility, headache, and cutaneous ulcers. They become chloro-anæmic and suffer from constipation. Several of them complain of being impotent. Aniline destroys red blood corpuscles and forms methæmoglobin. The urine is generally discoloured brown, or brownish black. The skin is faintly blue and occasionally the seat of an eruption. Few fatal cases of aniline poisoning have been recorded. In Dr. Fred. I. Smith's case the patient, a woman aged forty-two, had swallowed three ounces of marking-ink, of which aniline was the principal ingredient. Shortly afterwards she became unconscious, and remained thus until she died twelve hours after taking the poison; the symptoms and physical signs were purple lips, pale and bluish skin, small pupils, stertorous breathing, and full and slow pulse. The stomach was washed out, ether injected, and oxygen administered; but without avail. The blood is so changed by the action of aniline that it fails to take up oxygen. At the autopsy the lungs were found congested, and the heart relaxed and empty of blood. What quantity of aniline will prove fatal it is difficult to say. Anything over 1½ drachm would probably cause death; although recovery has taken place under treatment after 2½ drachms have been swallowed.

EXPLOSIVES: the dangers incidental to their manufacture and their use in coal mines—Roburite, Tonite, Melenite, Dynamite, Nitro-glycerine, and Gunpowder.

Since the "Explosives Act" 1875 came into operation, the growth of the trade of explosives in this country has been remarkable, owing to the introduction of smokeless powder and the increasing number of nitro-glycerine compounds that are being thrown upon the market. The Government Report for 1895 shows that 10,000 people are employed in their manufacture, and that whilst during that year 152 accidents had occurred, causing 40 deaths and injuring 167 people, most of the accidents happened under conditions to which the controlling provisions of the Act do not apply.

In the manufacture of high explosives *dinitro-benzole* is largely used. It reaches the factory in a purified state packed in casks in irregular lumps, or in the form of small slabs. The dinitro-benzole is first ground in an apparatus not unlike an ordinary mortar. During this process a considerable quantity of dust is given off, and the atmosphere readily becomes impregnated with the smell of bitter almonds. The yellow powder thus obtained is taken to the mixing-shed, where it is mixed with oxidising salts and heated. Subsequently when cool it is removed. It is at this stage of the manufacture that workmen are specially exposed to the vapours—the dangerous effects of which may be considerably lessened by the use of a fan. Next the explosive is taken to the cartridge-room, where women and girls are employed in filling cartridges. When these are filled they are taken to the dipping-shed, and rendered waterproof by being immersed in liquid paraffin and wax. The men who work in the "grinding" and "mixing" departments suffer from the effects of the noxious fumes; and in the cartridge department, where women and girls are employed, considerable risk to health is run, probably from handling the goods. Of the three varieties of dinitro-benzole which are known to chemists, only one is used in the manufacture of explosives, namely, *meta-dinitro-benzole;* but this is admitted to be a powerful poison, whether ingested, absorbed through the skin, or inhaled into the lungs as vapour or dust.

As the symptoms met with amongst those who are engaged in the manufacture of explosives are due to dinitro-benzole, the reader is referred to the preceding section for details of these. It is sufficient here to state that there is a dark blue colour of the skin, breathlessness, unsteadiness of gait, and amblyopia. In this section we are more specially concerned with the symptoms that occur in those whose occupation, such as coal miners and quarrymen, exposes them to the inhalation of smoke arising from the firing of explosives. Coal miners have complained of the deleterious effects of such explosives as roburite, tonite, dynamite, nitro-glycerine, and gunpowder. Tonite is composed of barium nitrate and gun-cotton in nearly equal proportions; roburite is an intimate mixture of ammonium nitrate and chlorinated dinitro-benzole in the proportion of 7 to 1. In the explosion of both of these substances the products formed are probably—for roburite, carbonic dioxide, nitrogen, water, and hydrochloric acid; for tonite, carbonate of barium, water, nitrogen, and oxygen. Gunpowder, on the other hand, is an intimate mixture of charcoal, sulphur, and nitre, and the products of its explosion are principally carbon dioxide and monoxide, nitrogen, and sulphuretted hydrogen.

Ross (84), in directing attention to poisoning by *roburite*, states that miners, after a prolonged and repeated exposure to the smoke arising from the firing of the explosive, complain of headache, frontal or occipital, dizziness, nausea and vomiting, constriction at the chest, fleeting pains in the trunk and limbs, numbness of fingers and toes—as if they were asleep, shortness of breath and palpitation on exertion, and loss of vision. To these may be added emaciation and drowsiness. The urine is deeply coloured like port wine. The lips are cyanosed, the face pale, the extremities cold, the grasp of the hand feeble, and there is slight loss of the power of opposing the thumb to the fingers. There is loss of power in the feet, so that the patient cannot stand or walk as formerly. The knee-jerk may be aggravated or absent; there are also loss of sexual desire, recurrent attacks of dimness of vision, and hyperæsthesia of the skin. Many of these symptoms are attributed to the improper handling of the cartridges by the men; but it has been shown that in many instances this was never done by miners who suffered; their illness, therefore, could only have been due to inhalation of the smoke in the mine. That the smoke is deleterious to coal miners has long been believed amongst themselves; and it formed the subject of a special investigation both in Northumberland and Lancashire. Ross alludes to the marked anæmia and the blue lips of men, otherwise healthy, who have been exposed to the fumes of roburite—physical signs which indicate that destruction of hæmoglobin has taken place within the blood-vessels; also to the muscular weakness, tingling of the limbs and sluggish patellar tendon reactions, as suggesting the early stage of peripheral neuritis: he therefore regarded the employment of roburite as harmful to the health of the miners. In Lancashire the subject was investigated by a special committee, and the opinion arrived at was that the nitro-benzene poisoning was due to the improper handling of the cartridges; and that where care was taken to have the shot fired properly, with free ventilation so that the fumes could speedily escape, the use of roburite was not harmful to the coal miners. Moreover, it was maintained that in complete combustion of the explosive no trace of nitro-benzene derivatives are left. The coal miners of the North of England having also objected to the use of roburite, the Durham Miners' Association undertook, with the assistance of Professor Bedson, Drs. Drummond and Hume, to solve the question whether the fumes produced from the use of roburite and tonite are injurious to health (100). The experiments were conducted in coal mines; the explosives used being roburite, tonite, and gunpowder. By means of aspirators Bedson removed air from the mines shortly after the shots were fired, and the result of his analyses showed the absence of deleterious gases in roburite smoke, and likewise in that from tonite. What struck Bedson in the fumes from gunpowder was their marked visibility compared to those of the higher explosives, also the distinct evidence of sulphuretted hydrogen. In some of the experiments where roburite had been fired there was a distinct odour of nitro-benzene in the atmosphere, although none was found chemically. The injurious substances present in the fumes from these explosives are carbon monoxide, nitric oxide, and sulphuretted hydrogen. The first of these compounds is produced by each of the explosives; and is generated both by the burning of the fuse and by the heated carbonic acid gas passing over the coal, whilst the sulphuretted hydrogen comes from the gunpowder alone. If carbonic acid is taken as a measure of the vitiation of the atmosphere, gunpowder and roburite have practically the same effect; whilst the vitiation from tonite is greater. Gunpowder smoke contains in addition carbon monoxide and sulphuretted hydrogen, both of which are injurious gases. As for carbon monoxide, tonite produces the most, gunpowder comes next, and roburite produces the least. The solution of the problem, so far as the use of these explosives in coal mines is concerned, is in the first place one of ventilation. One of the dangers of these high explosives is the fact that the fumes are invisible; and thus a coal miner might return to the particular part of the "working" sooner than he would if gunpowder had been used, the fumes from which are visible, in which more solid matter is suspended, and the odour of which is characteristic. The symptoms complained of by the Durham miners, and attributed by them to the firing of roburite, were those of "biliary derangement." Jaundice was occasionally present, and headache, vomiting, and drowsiness; but it did not appear that these symptoms were necessarily due to the use of the explosives, as the nitrobenzene vapours seemed to be present in too small a quantity to be injurious. Besides, many of the symptoms might just as properly be attributed to the ordinary conditions under which coal miners work, namely, in confined spaces, the air of which is fouled by carbon monoxide, consequent upon the firing of all kinds of explosives. The committee were particularly struck in this inquiry by the rapidity with which the symptoms complained of by the men disappeared. They were much milder, too, thanks to the excellent ventilation of the Durham coal mines, than the symptoms observed by Ross amongst the Lancashire pitmen. Under all circumstances where these explosives are used it is advised that the fuse should be fired by electricity, and that miners should not return to that part of the pit until at least five minutes afterwards.

Nitro-glycerine, Gun-cotton, Dynamite, Blasting Gelatine, etc.—The history of modern blasting agents can be briefly told. In 1847 Sobrero, an Italian, discovered the sweet viscous substance known as nitroglycerine. A little later, Schonbein of Bale, and Baron Lenck, an Austrian, simultaneously discovered gun-cotton. The opinion held by chemists that gun-cotton could only be exploded by detonation, and never by spontaneous ignition, was rudely shaken by the accidental firing of gun-cotton at the Stowmarket factory in 1871. It is the dangerous liability to spontaneous decomposition from heat which has removed this explosive from competition with others of the nitro-glycerine group. As nitro-glycerine under certain conditions is also liable to undergo spontaneous decomposition, Alfred Nobel, a Swedish engineer, sought for an absorbent capable of imbibing sufficient of the explosive to allow of nitroglycerine still remaining available for blasting purposes, but yet less likely to undergo spontaneous decomposition; of becoming, in fact, a comparatively harmless solid. In certain parts of Hanover Nobel found a porous siliceous earth, of low specific gravity, known as "Kisselguhr," composed of the remains of infusorial insects. Importing this "Kisselguhr" into the manufacture of nitro-glycerine he invented what is known as *dynamite*; a much safer article for transportation than nitroglycerine, and much more manageable as an explosive. To explode dynamite heat and strong percussion are necessary. Although a superior and safer explosive than nitro-glycerine Nobel did not rest satisfied with dynamite. For the "Kisselguhr," which he regarded as a weakening element, he substituted nitro-cotton, itself an explosive, and blending this with nitro-glycerine he obtained *blasting gelatine*. This latest explosive of Nobel's, blasting gelatine, is regarded as one of the "cheapest, strongest, and safest blasting agents known to chemistry."

Nitro-glycerine produces peculiar effects upon those who manufacture it. Dr. Dupré, analyst of explosives to the Home Office, informs me that, unlike dinitro-benzole, the effect is transitory; apparently bad effects are never left behind, or very rarely. The work-people suffer at first; but they soon become accustomed to the vapour without any impairment of health. If, however, they leave off work for a time, and again return to the factory, they invariably suffer as at first. In nitro-glycerine factories the men and women do not work on Saturday, as the last day of the week is employed for cleaning up; on resuming work on the Monday a large proportion of the workers invariably suffer for a few hours, the symptoms being extremely severe headache, accompanied by violent sickness and a prostration so extreme as sometimes to require the use of stimulants. Like amyl-nitrite nitro-glycerine dilates the blood-vessels. When nitro-glycerine preparations are properly detonated or exploded, the products are practically harmless; they are chiefly carbonic acid, water and nitrogen. If, however, detonation be imperfect, or if the explosive merely burns, the gases evolved contain much nitrous acid, some carbon monoxide, and perhaps other deleterious compounds. These products of incomplete detonation, particularly nitric oxide, are highly dangerous; and a number of fatal accidents due to them have already occurred in this country and in Australia. When symptoms arise on the inhalation of these fumes stimulants and rest in the recumbent position are called for. Potassium bromide is believed by many to have the power of preventing the attacks.

To the use of other well-known explosives miners have objected as in the cases of roburite and tonite. Dr. Arlidge quotes the case of a boy who inhaled for five minutes large quantities of the smoke slowly evolved from incompletely ignited *dynamite*. The fumes were pungent and suffocating, and resembled those of sulphur. The symptoms were vomiting and headache, followed by urgent dyspnœa and cyanosis; the patient died twenty-one hours after the exposure. Beyond pulmonary œdema and deep blue coloration of the bronchial mucous membrane, with punctiform hæmorrhages, nothing was detected at the autopsy. In another patient the symptoms, which arose on the day following the exposure, were semi-consciousness, very rapid pulse, quick breathing —the respirations reaching 96 in the minute—and the physical signs of congested lungs. The temperature was normal. Under the influence of rest, purging and sweating, recovery took place in four days.

The symptoms following the use of *sicareit* (securite, or sicherheit) resemble those which are caused by roburite; namely, headache, lassitude, cyanosis, rapid pulse, and the emission of deep brown urine.

The effects of dynamite are a sensation as if the head would burst, difficult breathing, and momentary unconsciousness; symptoms which rapidly disappear on exposure of the patient in the open air.

Picric acid is an essential constituent of several of the high explosives, such as melinite, for example, a secret explosive belonging to the French Government; and it is to the picric acid which it contains that the unpleasant symptoms caused by its use are attributed. In the manufacture of it nitric acid is poured upon phenol, and during the process fumes of nitrous acid are given off along with picric acid which, in its nascent state, causes dyspnœa, dry hacking cough, anæmia and debility. The vapour stains yellow the conjunctivæ, skin and hair; and causes conjunctivitis. The dyspnœa tends to become paroxysmal, and the cough may be followed by hæmoptysis. The nervous system and the other internal organs appear to escape. Melinite has not been used to any extent in coal mining, if at all.

Erb found that in rabbits 8 grains of picric acid produced a fall of the body temperature, diarrhœa, collapse and death, preceded by convulsions. Most of the tissues were stained yellowish red. The blood of animals thus poisoned was dirty brown in colour, and the white blood cells were increased in number. An urticarial eruption, resembling measles, is said to have been caused in men by picrate of ammonia. The urine becomes yellow, and there is a similar discoloration of the conjunctivæ and skin. If the dose be large, vomiting and purging occur.

The symptoms complained of by miners after the use of any of the above explosives may be summarised as headache, giddiness, derangement of the respiratory function, and great prostration.

CARBONIC OXIDE (COAL GAS AND WATER GAS) POISONING.—Carbon monoxide, CO, is a colourless, odourless, and tasteless gas, rarely found pure outside the chemical laboratory. It is usually found mixed with other gases; and it owes its extremely poisonous character to the fact that, when inspired, it enters into direct combination with the hæmoglobin of the blood, imparting to that fluid a bright cherry-red colour. It forms so stable a compound with the colouring matter of the red blood cells that they become incapable of carrying oxygen to the tissues. Thus is it that carbon monoxide is more dangerous than carbon dioxide. Carbonic oxide is present in the fumes emitted from charcoal stoves in which the combustion of the carbon is incomplete. It is one of the products of the combustion of coal, and is the gas which is seen burning with a blue flame in an ordinary open fire. It is one of the constituents of illuminating gas, and it is also present in the fumes escaping from coke ovens; tramps, who have sought the warm shelter of these ovens and lain down beside them overnight, may inhale them and fall into a heavy comatose sleep which occasionally ends in death. In France the fumes from charcoal stoves are frequently inhaled as a painless suicide. The fumes from these stoves are toxic in proportion to the amount of carbon monoxide they contain. Poisoning by carbonic oxide has been frequently confounded with that caused by carbon dioxide (carbonic acid). In the case of carbonic oxide the symptoms are those of a narcotic; the nervous system is gradually lulled into a sleep which ends in coma: whereas in carbonic acid poisoning there is usually greater disturbance of the respiration.

Inhalation of atmospheric air containing 1 to 2 per cent of carbonic oxide may cause not only unpleasant but very serious symptoms; and whilst the breathing of air loaded with a similar percentage of carbonic acid cannot be accomplished with impunity, the evidence is in favour of carbonic oxide being the more toxic; for life may still go on for a short time in an atmosphere containing 10 to 20 per cent of carbon dioxide. The rapidity with which carbon monoxide unites with hæmoglobin, and the stability of the carboxyhæmoglobin formed, render it a peculiarly dangerous gas. Although under these circumstances the blood has a bright cherry-red colour, it is quite incapable either of carrying or imparting oxygen to the tissues, and thus, internal respiration becoming impossible, the patient dies asphyxiated. When the blood in such a case is examined spectroscopically it shows two absorption bands between the D and E lines, that is, the yellow and the green. The spectrum is not unlike that given by oxyhæmoglobin, only the broad band is slightly nearer the violet end of the spectrum. Carboxyhæmoglobin is distinguished from oxyhæmoglobin in not being reduced by ammonium sulphide solution. Katayama, too, has demonstrated that whilst the addition of acetic acid and ammonium sulphide (with sulphur in solution) to normal blood produces a greenish gray or reddish green-gray colour, when they are added to CO blood a beautiful clear rose-red is produced (33).

Illuminating gas owes its toxic properties to the 5-10 per cent of carbon monoxide it contains; but in "water gas," which is prepared by acting upon burning charcoal with steam, there is frequently as much as from 30 to 40 per cent or more of carbonic oxide. This gas, which is also used for illuminating and heating purposes, and of which much was expected, is a mixture of carbonic oxide, carbon dioxide and hydrogen. As this gas has, practically speaking, no disagreeable odour its presence is less easily detected than ordinary coal gas. Its very large percentage of carbonic oxide makes it more prompt in its action and more dangerous than ordinary illuminating gas. So serious have been the consequences of the inhalation of "water gas," that some English public bodies have been obliged to do away with it. As carbonic oxide is odourless and tasteless, an individual may be gradually poisoned with it unawares. The presence of from 4 to 5 per cent of carbonic oxide in atmospheric air is fatal to small animals, and 10 per cent is fatal to man. Ordinary illuminating gas frequently contains from 5 to 10 per cent of carbonic oxide, the breathing of which from a leak in a gas-pipe or a tap left open, say in a bed-room overnight, has proved fatal. So insidious is it in its operation and so narcotising is its action that, if respired during sleep, the sufferer quietly passes into a state of coma which may be very profound; particularly if the gas has been breathed in small quantities and for a long time.

The symptoms vary with the amount of carbonic oxide inhaled. Usually, after experiencing a sense of discomfort with throbbing of the blood-vessels, the patient complains of severe headache, giddiness, and great debility. These may be followed by nausea and vomiting. A drowsy feeling may creep on, gradually leading to insensibility, preceded occasionally by convulsions and ending in delirium or coma. The pulse is full and bounding, respiration is acclerated and laboured, the skin dusky, the lips and extremities blue; and by degrees the patient dies asphyxiated. Should recovery take place convalescence is usually tardy, and its course is frequently interrupted by pulmonary or nervous affections. There may be loss of memory for some time afterwards, the urine may contain albumin or sugar, and the lungs be the seat of bronchitis or a low form of pneumonia. Scott of Tollcross reports the case of a man who suffered from dementia consequent upon carbon monoxide poisoning. Whilst engaged in the ammonia works connected with the blast furnaces of the Clyde Ironworks the man was found lying in front of one of the flues apparently dead. His face was ghastly pale, pupils dilated, breathing shallow and quick, pulse fairly strong but slow: he was completely insensible; but by degrees he became conscious, yet not until after several convulsions. Subsequently he became maniacal, and afterwards listless and apathetic. He had inhaled the "clear gas" that comes from the ammonia works, which Scott found, on analysis, to contain 25 per cent of carbon monoxide.

Haldane, dealing with the poisonous gases met with in the air of coal mines, draws attention to the presence therein of carbonic oxide, and shows how the quantity of carbon monoxide absorbed by the blood is influenced by the amount of oxygen present in the atmosphere. Carbonic oxide is more poisonous when air contains a diminished proportion of oxygen; and should carbonic oxide be present in atmospheric air in large quantity it may cause death with convulsions in so few seconds that the blood in certain parts of the body may contain very little carboxyhæmoglobin; death having occurred too rapidly for the whole of the blood to have become saturated. I have already stated that the presence of one per cent of carbon monoxide may cause unpleasant symptoms; but Hempel has shown that even such a small proportion as 0·06 per cent may have the same effect. Besides its interference with respiratory exchange, death in such small animals as mice seemed accelerated by a fall of temperature consequent upon diminished metabolism and heat production. Haldane has clearly demonstrated that in the presence of oxygen carbonic oxide is much less poisonous than it is in air, and that the poisonous action of carbon monoxide is increased by diminishing the oxygen percentage. When the oxygen tension is high the individual is not so dependent upon his red blood corpuscles for the carriage of oxygen, as a considerable quantity of oxygen may be taken up dissolved in the blood. There is a limit, however, to which the oxygen tension may be raised; for, as Paul Bert showed, at a tension slightly under five atmospheres oxygen itself acts as a poison.

After death by carbon monoxide the blood retains its bright cherry colour for a time, and when shaken it forms a froth of a violet colour. The skin and internal organs, as well as any post-mortem hypostases, exhibit a bright red colour. The lungs are frequently congested.

As regards treatment, immediate removal of the patient from the presence of the gas, and artificial respiration persisted in for hours in order to expel, if possible, the poison from the blood, rhythmic traction of the tongue, inhalation of oxygen, hypodermic injections of strychnine, and the application of the faradaic current to the phrenic nerve, are called for; but even with these measures venesection and transfusion of healthy blood may also be necessary.

Haldane has conclusively demonstrated that, in colliery explosions, whilst many of the miners are killed by the force of the explosion, many meet their death by inhaling the "after-damp"—a gas which contains varying quantities of carbon monoxide. The proof of this gas having been the cause of death rests in the pink colour of the skin, a reddening of the face and hands—which gives the bodies an extraordinary appearance of life—and the result obtained by spectroscopic examination of the blood. To the collier working in the pit the presence of carbonic acid (CO_2) or "choke damp" is made known by the extinction of his light, and by a slight embarrassment of his breathing; but carbon monoxide gives no such warning. Alike in those who are working in the recesses of the mine, and in rescuers who descend into the pit after an explosion and are brought into contact with "after-damp," there are the same symptoms—drowsiness, extreme debility, and unconsciousness. Since mice are easily killed by carbon monoxide Haldane has suggested that they should be carried into such underground chambers as are supposed to contain carbonic oxide gas; and as these animals have a respiratory exchange twenty times as rapid as that of man there would be an interval of several minutes (varying from 12 to 40), after death of the mouse, sufficient to allow the miner to escape. When a colliery explosion has occurred it is absolutely necessary to get fresh air as rapidly as possible into the pit; for although miners may have breathed the "after-damp" and been rendered unconscious by it, death may not supervene for an hour or more. Rescue parties should descend, and, in order that they may remain within the limits of safety, they should carry with them mice and cylinders of oxygen. Artificial respiration, inhalation of oxygen, removal of the miners to bank as early as possible, the administration of stimulants, and maintenance of bodily temperature are necessary.

LEAD POISONING.—Of the various forms of metallic poisoning that caused by lead is the commonest and most subtle. In five years ending 1890 there occurred 1822 deaths from accidental poisoning in England and Wales; of these, 541 were due to lead, 17 to arsenic, and 36 to phosphorus: that is to say, 29 per cent of the total cases of deaths from poisoning were due to lead; figures which, when compared with the five years ending 1880, show an increase of nearly 9 per cent in the latter period.

Lead poisoning occurs in isolated cases; or it may assume an epidemic character. Mere handling of the metal for a long time, or inhalation of the dust of the various salts of lead, may be followed by symptoms of poisoning. It has been caused by the accidental or criminal adulteration of food and drink. People are not equally affected by it. There is not only an individual idiosyncrasy—some persons being more susceptible than others—but there is an hereditary disposition to suffer from lead; and to this may be added a sexual idiosyncrasy, as women—particularly young women—fall more easily under the influence of lead than men.

Lead poisoning is not a modern disease; it has been known for centuries. It is described under various names, for example, plumbism, saturnine poisoning, colica Poitou, colica Pictonum, and, lastly, colica pictorum, from the Latin word *pictor*, a painter.

Setting aside for the moment the industrial forms of lead poisoning, that induced by contaminated drinking-water is the most important. All at once large numbers of people may be stricken with symptoms of plumbism. In such epidemics the gathering-ground has frequently been moorland, the water on which, as it trickles through the peaty soil or comes into contact with decaying leaves, takes up humic acid: this acidified water acts upon the lead of the conducting pipe or the cistern and dissolves out some of the metal. Some chemists maintain that this action on the leaden pipes is aided by the presence of iron in the water, which gives it an acid reaction and makes it soft. Distilled water acts upon lead, because it is impossible to remove therefrom all traces of organic matter. The presence of nitrogenous compounds confers upon water a solvent influence upon lead—the oxidation of the metal being brought about by the oxides of nitrogen, which, in the form of nitrites, act as oxygen-carriers between the air and the lead. When distilled water acts upon lead it produces a solid white compound, the oxyhydrate; but thus acting alone upon lead it cannot give rise to the oxyhydrate, which is a compound molecule requiring one molecule of water and two extra atoms of oxygen. The hydrogen of the water must be displaced either by high temperature or by the lead receiving oxygen; and the most frequent source of the oxygen are the nitrogenous compounds in the water in the form of nitrates. If the water is exposed to the air, a small quantity of nitrate is quite sufficient; for the process is one of continued deoxidation of the nitrate by the lead, and of reoxidation by the oxygen from the air. The proof of this series of deoxidations and reoxidations and that the nitrates are the source of the oxygen, is that if lead be placed in water containing a nitrate the nitrate is rapidly reduced to nitrite. Nitrogen oxides are almost invariably present in water: they arise from the decomposition of organic compounds in which the operation of micro-organisms probably plays an important part. The oxyhydrate of lead, already alluded to, is very insoluble in pure water; but if the least trace of acid be present, or certain salts, such as nitrate of ammonia, it is freely soluble.

Garrett found, when distilled water has acted upon lead for 84 hours, that it contains $\frac{1}{100}$ grain of metallic lead per gallon; that if one grain of sulphuric acid per gallon were added, in 84 hours it contains $\frac{1}{8}$ of a grain, whilst the same quantity of nitric acid gives $\frac{1}{3}$ of a grain in an equal period. The retention of water in a lead service pipe overnight may therefore allow of the solution of a fairly large quantity of the metal — which explains the fact that many of the victims of plumbism have been persons who drank the water first removed from the pipe in the morning. It is thus, too, that barmen and barmaids have suffered by taking regularly the first swill of beer which has been in the tap overnight. A short time suffices for liquids thus to become contaminated. Water kept in contact with a lead pipe for half an hour has been found to contain $\frac{1}{10}$ grain, at the end of an hour $\frac{1}{3}$ of a grain, and at the end of 12 hours 1·4 grain per gallon. The presence of a very minute trace of lead in drinking-water is sufficient to cause serious symptoms. Experience shows that if lead is introduced into the system in very small quantities, and for a long time, it is more likely to cause serious symptoms than when it is taken in larger doses and only on a few occasions. Cases illustrating the poisonous doses of lead are quoted by Dr. De Chaumont (in which the water contained $\frac{1}{20}$ grain per gallon); Dr. Hunter of Pudsey ($\frac{1}{15}$ to $\frac{1}{20}$ grain); Dr. Angus Smith ($\frac{1}{100}$ grain); Dr. Adams ($\frac{1}{100}$ grain); Dr. Sydney Ringer ($\frac{1}{50}$ grain): in one of Dr. Dixon Mann's cases the drinking-water contained 2·4 milligrammes of lead per litre, and in one of my own cases serious symptoms arose from drinking water which contained 0·0028 grain of lead per gallon. Of the family of Louis Philippe, at Claremont, 34 per cent who drank the water, which contained $\frac{7}{10}$ grain per gallon, suffered from plumbism.

During the action of water upon lead the crystalline oxyhydrate of the metal is formed. If certain salts are present in solution there is a transference of portions of the acid radicles to the base, resulting therefore in the formation of salts of lead other than the oxyhydrate. Salts of lead more soluble than the oxyhydrate may thus be formed; for example, nitrate, nitrite, or carbonate. The presence of carbonic acid increases the solvent influence of water upon lead. The oxyhydrate first formed by the water is dissolved by the carbonic acid present, and a considerable quantity of lead may thus pass into solution as acid carbonate; but as the formation of oxyhydrate continues, the carbonic acid is neutralised, and there results a basic carbonate of lead which is insoluble and is deposited upon the surface of the pipe, forming a protective covering whereby further action of the water is at least retarded if not prevented. Under these circumstances the addition of alkaline carbonates to water may prevent lead poisoning. Water acts with greater vigour upon a new than upon an old lead pipe; for on the surface of the latter a protective covering of the dehydrated oxide or carbonate may be present: both of these, however, are readily dissolved when the water becomes slightly acid, or when its temperature is raised; hence the danger of using water for culinary purposes first drawn from the kitchen boiler in the early morning. It has been stated as an offset against this danger that if tea be made with water containing a trace of lead the metal is discharged, but experiment has shown that there is no truth whatever in the statement; moreover, there is the risk that the tea itself may have been contaminated by a wrapper of leaden foil. In one experiment with water containing $\frac{1}{24}$ grain of lead per gallon, the tea infused from it contained $\frac{1}{23}$ grain.

The drinking-water in our houses should be free from such contamination as we have been considering. Water that naturally contains carbonate of lime is not acted upon by lead; and we have seen that the addition of alkaline carbonates is a preventive: so are alkaline phosphates and silicates. When water has filtered through a bed of sand it is not so liable to be contaminated by lead in its transit through the pipes, as the water takes up a certain amount of silica, which unites with any dissolved lead to form an insoluble silicate, and this forms a coating on the inside of the pipe. To diminish the possibility of plumbism, drinking-water should not be allowed to remain in contact with a lead pipe: in the early morning the tap should be allowed to run freely for a time. To get rid of this form of poisoning altogether we should abolish lead pipes for conducting, and lead cisterns for storing water. Iron pipes lined with tin, or lead pipes lined with glass, are desirable substitutes. To cause plumbism it is not necessary that the drinking-water should contain lead in solution. One of the most serious cases of saturnine poisoning observed in my own practice was that of a lady in Kensington, seen in consultation with Mr. Berkeley of Wimpole Street and Dr. Cayley, who with one of her sons suffered severely from using water taken from a cistern in which several loose lumps of white lead had been left by a careless workman. The water as it flowed from the cistern was muddy: it contained a large quantity of lead in a precipitated form, but none in solution. Lead had been deposited upon vegetables boiled in this muddy water, and thus it gained an entrance into the system.

When drinking-water contains lead, the addition of sulphuretted hydrogen or ammonium sulphide at once precipitates the metal as a dark brown sulphide—care having been previously taken to add a small quantity of hydrochloric acid to it to precipitate any iron that may be present. Should there be only a minute trace of lead in the water the addition of a small quantity of barium sulphate ($\frac{1}{2}$ grain) allows of the precipitate coming down in two layers: the lower stratum forms rapidly, and is composed of denser particles, whilst the upper, being lighter, takes a longer time to subside; in this the sulphide of lead is deposited. A buff or dark brown colour is thus imparted to it, which causes it to stand out in distinct contrast to the under-lying well-defined white layer. By this means $\frac{1}{200}$ grain of lead per gallon may be detected. Occasionally it is necessary to test the "plumbo-solvency" of a suspected water, and for this purpose nothing is better than the "shot" test of Whitelegge, namely, filtering the water through lead shot specially prepared free from arsenic and then testing it.

We have dealt at length with the question of epidemic plumbism, for the disease has rather increased than diminished of late; and it will tend to become even more prevalent as our rapidly growing town-populations go far afield in search of water. Moorland waters, in the late summer and autumn months, are strongly impregnated with peaty acids. Water, according to Power and Houston (75), may simply dissolve lead by a true plumbo-solvent action, or it may possess an "erosive ability," whereby it forms an almost insoluble lead compound so loosely attached to the lead as not to shield it from further attack. Distilled water possesses the first power, moorland water both; and although boiling may destroy the property possessed by distilled water, moorland waters remain unaffected. It has been demonstrated by Houston that two kinds of bacteria, probably derived from peat, are present in moorland water, which organisms are capable of generating an acid which imparts to water its power of dissolving lead.

Lead salts are all more or less poisonous. Even so insoluble a salt as the sulphate is acted upon by the intestinal juices. It is the custom in white-lead works to supply an acid lemonade composed of sulphate of magnesia, sulphuric acid, and fresh lemons to the work-people in the hope of preventing colic; on the supposition that the lead carbonate is converted into sulphate, which, being insoluble, is passed out with the fæces. To some extent this is true, but even the sulphate is more or less soluble. In my own experiments animals that received sulphate of lead died, and in their liver we found lead. The sulphide of lead is very insoluble; hence the preventive treatment of plumbism by giving sulphur in milk. Chromate of lead is also very insoluble, and yet it has frequently caused poisoning by diffusion as fine dust through the air in the carding-rooms of woollen or cotton factories, effects which have disappeared at once on the introduction of fan ventilators.

Lead finds its way into our victuals when these are cooked in cheap enamelled or tinned ware, and in the adulteration of articles of diet, for example, flour or pastry coloured yellow by cheap baking powder, wines, beer, and cider, tinned meats, and tea wrapped in leaden foil. The latter is a source of danger owing to the excessive tea-drinking of the labouring classes. It is only right to add that lead has not always been found in tinned jellies and meats, although present in the solder.

Industrial lead poisoning claims many victims annually owing to the inhalation of dust, the swallowing of impregnated saliva, eating with unwashed hands in the workshop, the adhesion of lead dust to the clothes of the work-people, or to the solution of it in the sweat and absorption by the skin. Improved ventilation of factories, attention to stringent rules of cleanliness, restriction of female labour, and a medical examination of the work-people on first entering the factory, and afterwards at weekly periods, have done much to diminish industrial plumbism; but the abolition of all hand-work and the manufacture of lead by electrolysis is highly desirable.

Lead mining in this country is no longer the extensive industry it was of yore. It is still pursued in some of the dales of Durham, Yorkshire, Cumberland, and the peak of Derbyshire. Foreign ores, particularly the Australian and Spanish, are richer in silver than ours, so that at the present time most of the metallic or pig lead used in this country is imported. English lead-ore seldom contains more than eight or ten ounces of silver to the ton; but in Spanish there may be 40 to 80 ounces to the ton; in Greek ore 80; whilst in Australian ore it may run as low as 60 ounces, or as high as 400 to 500 ounces; in some instances it has even run 1000 ounces to the ton. The process of desilverisation cannot be regarded as an unhealthy one to the operative. The silver is extracted by the zinc or Parke's process, the principle of which is that in smelting the ore zinc alloys itself with silver and floats on the surface.

The British lead miner runs little or no risk from plumbism. The getting and handling of the ore is unattended by such symptoms as colic, headache, or paralysis; as in this country the lead in the mines is almost pure metal mixed with spar. In the Broken Hill mines of Australia the ore exists in the form of carbonate; and many of the miners there, as also in Italy, have died from lead encephalopathy. The lead miner in this country, however, runs other risks. The mines in many instances are deep, damp, and badly ventilated—and the ingress and egress are difficult. The men become prematurely old: they suffer from cough and spit. Many of them die of phthisis, in which the lungs present the characters of fibroid change. In the indurated lung we find no traces of lead, but tubercle bacilli are in the expectoration. Many of the lead miners also suffer from distorting rheumatic affections of the joints.

The dangers of plumbism arise during the smelting of the metal; but of late this has been diminished by placing a hood in front of the furnace, and by free ventilation. Nevertheless lead smelters are pale, and occasionally suffer from colic. But there is a more widely spread danger than that to the smelter. The white fumes that issue from the stack contain large quantities of lead; and, as the lead is deposited on the soil, cattle grazing in the neighbourhood have suffered and died from plumbism, the disease being spoken of as "bellond." Moreover, the flues from the smelting stacks have to be cleaned out from time to time; and the men who enter them for this purpose suffer from severe headache and giddiness. The remelting of old lead is not without danger; and as this is frequently carried on in small shops or private houses, people living in the immediate neighbourhood have shown symptoms of plumbism, and pregnant women and animals miscarry. In the fumes emitted from the chimneys, lead, zinc, manganese, and arsenic have been found. The melting of old lead pipes is then, in my opinion, much more dangerous than smelting the ore, owing probably to the large quantity of lead carbonate or organic compounds present. A similar danger attends the breaking up and burning of old railway carriages.

The white-lead factories supply the largest number of cases of plumbism. Lead poisoning also occurs among potters, who dip their ware in glaze, and amongst enamel-plate makers and tinners of cheap hollow ware. Metallic lead is not so dangerous as its salts, and yet the file-cutters of Sheffield who hammer their files upon a lead cushion frequently suffer from plumbism. The more soluble the salt of lead the greater is the danger. White lead or carbonate is the most harmful owing to its extensive employment, and it is on this account that various substitutes have been tried for it; but for purity, whiteness, and durability on exposure it is still superior to all pigments. White lead is usually made in this country by what is known as the old Dutch process, for the details of which chemical text-books are to be consulted.

House-painters suffer from plumbism. In burning off the old paint there is usually considerable stithe; inhalation of which causes colic, vomiting, and severe headache with constipation. This predisposes the individual so far that he readily succumbs to a fresh invasion of the poison. It is not so much the use of the brush and inhalation of the terebinthinated lead vapour that affects house-painters. Several coats of paint, for example, have to be applied. After the processes known as "prime" colouring and "puttying" with white lead comes the "flat" colouring. It is when these coats are dry that the painter, using sand-paper to make the surface flat, creates a cloud of dust, inhalation of which is frequently followed by colic or wrist-drop.

Lead gains access to the system by the skin, the respiratory passages, and the intestinal tract. Animals whose skin has been smeared with oleate of lead have died; the long-continued application of medicated plasters and the use of cosmetics and hair-dyes containing lead have caused plumbism, also the frequent handling of metallic lead. The metal or its salts in the form of dust may enter by the respiratory channels; the salts, becoming deposited by the alkaline juices of the respiratory passages, are first converted into carbonate and then into the more soluble bicarbonate. When lead has thus gained access symptoms are quickly induced, and they are usually more severe than when the metal has been swallowed. Entering the gastro-intestinal canal, it is acted upon by the gastric juice, the hydrochloric acid of which is sufficient to convert a quantity into soluble chloride. It has been demonstrated that during the simultaneous digestion of proteid a very small quantity of lead only is dissolved (68). Lead salts are also dissolved by bile, but if bile is allowed to act upon fat at the same time very little of the salt enters into solution. We have found pancreatic juice inactive upon lead. It is the hydrochloric acid of the gastric juice that is the active agent. When, therefore, lead salts have passed out of the stomach along with the acid chyme, there is nothing in the intestine, except bile, likely to act upon them—unless it be the acid products of bacterial life—and as sulphuretted hydrogen is always present in the intestinal canal, there is the probability that an insoluble lead sulphide will be formed, and thus eliminated. Plumbism is more likely to arise where very minute quantities of lead are repeatedly taken into the system than after a few larger doses. Small quantities are more completely dissolved, and are therefore more readily absorbed.

It is with plumbism as with intoxication in general; certain circumstances intensify the disposition to it: the younger the age the greater the liability, and particularly is this the case with women. Young women who are anæmic and ill-nourished are rapidly brought under the influence of the metal, and in them the nervous system is especially apt to suffer. In one of my own cases a month's work in a white lead factory proved fatal to a girl. In five years ending June 1889, 135 cases of lead poisoning were admitted into the Newcastle Infirmary: of these 91 were women and 44 men. The susceptibility of women was exhibited from the ages of 18 to 23; the largest number of admissions being at 19 and 22 years of age: the greatest susceptibility of men was from 41 to 48. In a second five years' series of admissions ending June 1894 the largest number of female admissions was at the ages of 19 and 25; and whilst males showed a tendency to suffer at 26, the larger number occurred after 40 years of age.

The drawing or emptying of "stoves" is regarded as the most dangerous part of white-lead making. When a girl has drawn a few stoves she will generally be found pale and listless, complaining of headache, a metallic taste in her mouth, and a distaste for food. Improper feeding, general destitution, and previous illnesses, alcoholic intemperance, and working in a badly ventilated factory, are circumstances which, with menstrual irregularities, strongly dispose young women to lead poisoning.

Lead poisoning occurs in four forms. In the first colic is the most important symptom; in the second the central nervous system is profoundly affected, the patient being the subject of epileptiform seizures called "lead encephalopathy"; the third is the neuro-muscular form, in which "drop-wrist" is the most marked symptom; and in the fourth are included all those cases of chronic plumbism characterised by profound cachexia, early decrepitude and albuminuria.

Colic is usually one of the earliest symptoms of lead poisoning, but it is generally preceded by anæmia. One of the earliest indications of plumbism is a peculiar anæmia or cachexia—the face becomes pale, and there is complaint of inability to take food, particularly in the morning, a metallic taste in the mouth, and of sickness, with or without constipation. If these premonitions are disregarded the patient is sooner or later seized with acute abdominal pain, usually paroxysmal. Colic, as a rule, is accompanied by constipation, but not necessarily so. The bowels may be fairly regular, very constipated or slightly loose. Usually there is constipation, and that, too, of an obstinate character. The abdominal pain may be so severe that the patient cannot allow the abdomen to be touched. In other cases relief is obtained by firmly pressing the abdomen, or by applying warmth externally. The pain of lead colic has a double character: it is paroxysmal, or it is constant and more of a dull aching. Days after the superficial or paroxysmal pain has subsided deep pressure upon the abdomen elicits signs of suffering, and the peculiarity of this pain, and sometimes too of the colic, is that it is either limited to one side entirely, or is more acutely felt on pressure on one side than the other. Frequently localised near the umbilicus, it may extend as far out as the external border of the rectus muscle; or it may be diffused over the upper half or two-thirds of the abdomen. The muscular walls are generally hard and retracted, but not necessarily so. The one-sided localisation of the pain is notable; for concurrent with this peculiar localisation of the abdominal pain I have frequently noticed that extreme pain is felt when firm pressure is made upon the line of the vagus in the neck, particularly on the corresponding side. It is interesting to note, too, that during recovery the disappearance of the vagus pain in the neck is contemporaneous with that which was elicited by pressure on the abdomen. Moreover the pupils are generally unequal; the rule, though not an invariable one, being that the pupil on the same side as the abdominal pain is smaller. The radial pulses also are unequal, that on the affected side being stronger or weaker as the case may be. In addition to colic, there is pain in the muscles of the arms or legs. The knee-jerk is usually exaggerated on the affected side. Even when the colic is distributed all over the abdomen the pupils may be unequal; one or both may be dilated, and there may be the inequality of the pulse already described.

Constipation generally accompanies the colic, but relief to pain does not immediately follow the action of the bowels. For several days, even though the bowels are being moved by aperients, pain may still be complained of and vomiting may continue. When the colic is severe the patient looks thoroughly ill; the face wears an expression of suffering, he rolls about in agony, and is with difficulty restrained. This peculiar restlessness is characteristic of acute lead colic.

It is difficult to explain the colic. Some authors believe that lead acts primarily upon nerve ganglia; others upon the muscular fibre of the intestinal wall, or upon the musculature of the intestinal arteries. Dr. Haig attributes it to the deposit of an insoluble lead urate, and therefore administers sodium salicylate. In animals that have died from plumbism I have found the small intestine irregularly contracted; at places so extreme was the spasm that the intestine felt like a piece of cord—its calibre being obliterated. Was the contraction of the intestine in these cases due to the direct action of lead upon the muscular fibre, or had the arteries become contracted primarily, and thus, by shutting off the blood-supply, caused nervous excitation and muscular contraction? Clearly the pain is due to extreme spasm of portions of the intestine and pressure upon sensitive nerves—and the recurrent pain would be explained by the effort of the dilated segments of the intestine to pass on their contents into the constricted portions below. Spasm and arterial ischæmia, by cutting off the supply of liquid, would aggravate constipation. It is probable that the nerve ganglia are first affected.

Accompanying the colic we find—(i.) the radial pulse extremely small, almost imperceptible; or it is hard and resistant: (ii.) oliguria—the secretion of urine is reduced to a minimum. The pulse may be as low as 40 to the minute. An extremely feeble pulse is characteristic of this period; so feeble is it that even the sphygmograph may fail to register it, and yet during colic there may be heightened arterial blood-pressure which comes and goes with the pain. It is no uncommon thing for colic to disappear and reappear; and this change is accompanied by relaxation and heightening of the arterial tension. The small amount of urine secreted during colic is noteworthy. It may fall as low as 8 to 12 ounces per diem, and in young subjects, particularly in first attacks, it is free from albumin. Except that it contains too little urea the urine at this stage, although lessened in quantity, presents no special feature. When the colic disappears, not only does the quantity of urine rise, but the urea as well. If saturnine colic is unaccompanied by complications the patients gradually recover, although in the early stages there are apt to be remissions. The mortality in this condition is less than 2 per cent.

In plumbism the face is usually pale: in the chronic forms the face is rounded, the features are expressionless, and the *anæmia* passes into a cachexia which may never disappear. On the gums may be observed a bluish black line along the margins close to the teeth; this is absent, however, if the teeth have fallen out, and in people who have regularly used the tooth-brush. It is frequently associated with ulceration and retraction of the gums, so that the teeth appear elongated and discoloured. Running up between the teeth may be seen small pyramidal masses of gum with well-defined blue margins. First described by Burton, the presence of the *blue line on the gums* is a considerable aid in diagnosis; and yet it may be present for months in the gums of lead-workers who are not suffering from plumbism. Its persistence, however, is an indication of the presence of lead in the system. Other substances besides lead may cause a line on the gums. I have seen a deep black line on the gums of a coal miner. In people who have been taking bismuth or copper, and whose teeth are decayed, a livid line is occasionally met with; in a child poisoned by tetrachloride of gold Stevenson found a purple-black line at the junction of teeth and gums. A delicate blue line is sometimes noticed on the gums of work-people exposed for a few hours to an atmosphere laden with lead dust; but, as it disappears on rinsing the mouth, it is a deposit of sulphide of lead on the mucous membrane and not in it. The characteristic blue line occurs at the margin of the gum where it is not in complete apposition with the teeth; and it is usually more pronounced on the lower than the upper gum. The presence of bad teeth, ulcerated gums, and want of cleanliness favour its establishment. In a few days after exposure to the poison the line may appear, and it persists. Its disappearance is not perceptibly hastened by friction or by the use of mouth-washes; nor is it quickly removed by medicines. The shortest times in which I have noticed its disappearance are from two weeks to four months. On other portions of the mucous membrane of the mouth bluish black patches may be observed; a frequent site of them being just inside the lower lip. It has been stated that the administration of potassium iodide in a case of plumbism will bring out the blue line if absent; but we have no proof of this. On microscopical examination of the gum numerous black granules of sulphide of lead are observed in the deeper cells of the epidermis, and not, as Fagge taught, in the small blood-vessels.

As regards the pallor, which is nearly always present, or the well-marked saturnine cachexia of the older cases, the blood is deficient in red cells without any increase of the white. The thyroid gland is extremely small, and in old cases there is atrophy and degeneration of the marrow of bones. Lead is frequently found in the bones.

It may be partly owing to the anæmia, and to the peculiar effects of lead upon menstruation, that women are more susceptible than men; and at an earlier age. This is not because women are more exposed to the specially dangerous processes in the manufacture of white lead. Menstruation is apt to be increased; but whilst in many cases there is menorrhagia every two or three weeks, in not a few there is amenorrhœa. Some writers attribute the headache, so frequently complained of by female lead-workers, to the scanty menstruation. It may aggravate it, but it is not the cause of it, for headache is equally a symptom in plumbism where there is menorrhagia. *Pregnant women readily abort.* So frequently is the tendency to miscarry exhibited by female lead-workers, that the only means sometimes by which the full term of pregnancy can be reached is to leave the factory altogether. This tendency to miscarry is equally well seen in the lower animals under experimental plumbism. Rabbits readily thus abort. In the lower animals the influence of sex in increasing the susceptibility to plumbism is just as noticeable as in the human female. In the female sex generally, not only is metabolism less active, but excretion is not so well performed: women, for example, suffer more from constipation than men; and though they pass relatively as large a quantity of urine as men, it has a lower specific gravity, and is relatively deficient in solids, particularly in urea. The elimination of nitrogen, therefore, is not so perfect as in men, and it is disturbed by the return of each menstrual period. Add to the effects of diminished nitrogenous metabolism and to variations in renal excretion those of constipation and irregular, profuse, or scanty menstruation, and we probably have the explanation of the greater susceptibility of women to lead poisoning than of men.

The nervous system is peculiarly prone to be affected by lead, and the extent to which it is affected is a measure of the menace to life. Colic or wrist-drop usually precedes cerebral symptoms in plumbism; but in many cases the only premonitory symptom is severe headache, during which the *tâche cérébrale* may be obtained; and then without further warning, of aura or otherwise, the patient is suddenly seized with a fit of varying severity and duration: this passes off, only to be repeated with increasing severity, until the patient passes into a state of coma from which he may never rally. Epileptiform seizures may be the only symptom of plumbism; but in other cases colic, wrist-drop, and fits are present at the same time. To the epileptiform seizures the term "lead encephalopathy" is applied, and of all forms of plumbism this is the most dangerous. It is the most fatal form, and in young women it is frequently preceded by symptoms which appear to be of a hysterical nature. So slight and seemingly functional are these hysterical symptoms that they have frequently thrown careful observers off their guard. Gradually they have deepened and been succeeded by epileptiform seizures, and within two days the patient has died. Debove and Achard applied the term "toxic hysteria" to those cases in which a neurosis arises under the influence of intoxication. Occasionally in plumbism hysterical paralysis is met with, accompanied by hemianæsthesia and amblyopia on the same side and anosmia on the opposite. Yet we do well to remember that saturnine toxic hysteria is frequently the forerunner of a very fatal form of lead poisoning. In lead encephalopathy the fit may only last a few minutes, consciousness being rapidly regained. The patient is usually very restless; there is great excitement, amounting to delirium, or there are dulness and melancholia. In the intervals the pulse is sometimes so feeble as scarcely to be felt; the secretion of urine falls—3 or 4 ounces only being secreted in twenty-four hours—and it may contain albumin. The fits, however, keep recurring, and in one of them the patient dies, or he may recover; but his vision has become affected to the degree of complete or incomplete blindness; or aphasia may be present.

In the neuro-muscular form the patient, after having experienced pain or numbness in the muscles of the forearm and leg, and perhaps too, but not necessarily, one or two attacks of colic, suddenly or gradually loses the power of his wrists; the hands fall powerless from the wrists, or the arms from the shoulders, and he lies in bed with hands crossed, unable to feed and clothe himself. This is the milder form of lead paralysis. The extensors are more liable to be affected than the flexors. The paralysis is usually bilateral, one side, however, being generally worse than the other. The muscles of the calves are tender to the grasp. There is rapid muscular atrophy. Occasionally the paralysis is widely distributed, the muscles of the trunk, back, and shoulders become affected and are painful on pressure. The paralysis may gradually disappear, or it may persist.

In the fourth form are included the victims of chronic plumbism. They present the history of a long exposure to lead and repeated attacks of colic; possibly, too, of wrist-drop and of one or two epileptic seizures. The patient is extremely cachectic; the metacarpo-phalangeal joints may be swollen, or other joints may be the seat of gout or rheumatism. The extensor muscles of the wrists and fingers may be atrophied. There is general malnutrition; the gums are ulcerated, and probably show a blue line; the sight is defective; the urine contains albumin; the health gradually fails; the individual is prematurely old, and he dies from some intercurrent disease. At the post-mortem the heart, kidneys, liver, and arteries are found to be the seats of pathological change.

Paralysis is usually regarded as a symptom of chronic plumbism; but it may occur in the acute form without being preceded either by colic or headache. The loss of power precedes the atrophy—when wasting once begins it advances rapidly. Paralysis of the extensor muscles of the wrists causes "wrist-drop," but it is noticed that the extensors of the fingers are also similarly affected—not all equally, however; the index-finger, for example, may not be so deeply paralysed, and consequently it recovers more quickly than the others. The flexors of the fingers, too, generally become paretic; so that when any effort is made to extend the fingers the flexors imperfectly contract and are thrown into a state of tremor. The supinator longus as a rule escapes; but if the muscles of the upper arm become affected this muscle is not exempted: supination of the hand is accomplished by an external rotation movement of the shoulder and a throwing-out of the hand by the patient. The index-finger may be affected, whilst the little finger escapes; or the thumb may not be so easily extended, its abductor and adductor muscles being paralysed; the fingers probably cannot be separated; the interosseous grooves deepen, and the back of the forearm becomes flattened in the muscular atrophy.

Whilst lead has a strong predilection for the muscles already mentioned, these may escape, and those of the upper arm be attacked; namely, the Duchenne-Erb group—the deltoid, biceps, brachialis anticus, and supinator longus. To this group is generally superadded paralysis of the supra and infra-spinators. This form of paralysis is usually bilateral, and occurs in the more inveterate types of lead poisoning. Of this group of muscles sometimes the deltoid is the only muscle affected, as in a case reported by Dr. Buzzard; in others only the supinator longus. When the whole group is affected the patient is unable to lift his arm—it hangs powerless by his side: he cannot bend the forearm at the elbow owing to paralysis of the biceps, and yet he can extend it, the triceps having escaped. It is said that in this state muscular atrophy and the disturbances of electrical contractility are less pronounced than in the more classic form. In one of my female patients not only was the Duchenne-Erb group of muscles affected, but there was also paralysis of the supinator longus and of the extensors of the wrists and fingers: the muscles of the pelvis, legs, and feet also became weak. It was a mild form of an acute multiple paralysis, accompanied by severe pain and rapid atrophy; it resembled the widely-distributed paralysis met with in polyneuritis, both as regards pain in the muscles, the distribution of the paralysis, and the rapidity of its development: the knee-jerks, however, were exaggerated. In fatal cases the paralysis invades the muscles of respiration—for example, the intercostals, the diaphragm, and the muscles of the larynx. The muscles concerned in deglutition, too, become affected; so that the patient lies in bed in the dorsal decubitus, perfectly helpless and unable to eat. Before the legs become paralysed the muscles are usually tender and the knee-jerks exaggerated. In one of my chronic cases the symptoms closely resembled those of bulbar paralysis: the tongue gradually became smaller, and speech and swallowing difficult; but there was never the dribbling of saliva met with in the classic medullary lesion, although the patient died of a subacute pulmonary affection.

In the early stages the skin is frequently very sensitive to the prick of a pin; but later it may become analgesic or anæsthetic, always bleeding, however, when pricked—a circumstance that removes it from the category of hysteria. According to Guinon the anæsthesia may be confined to those parts that have been brought into direct contact with lead; or it may be widely distributed, amounting to hemianæsthesia. Frequently there is tremor of the affected muscles, also of the naso-labial and of the tongue. In one case Buzzard found the third nerve affected, causing ptosis, with abolition of movements of the superior, inferior, and internal recti muscles; the pupil was dilated and did not react to light. The external rectus alone may be paralysed. Diplopia was observed in some of my own cases without any apparent muscular defect; nystagmus also. The musculature of the bladder may become affected, causing incontinence.

One of the gravest effects of lead upon the nervous system is *neuro-retinitis.* This may set in rapidly without any concurrent kidney disease. It is often associated with headache and epileptiform seizures. Vision may be very slightly obscured, or it may be lost temporarily or permanently. Attacks of transient blindness occur in the absence of neuro-retinitis, and seem to be central in their causation, probably toxic, or due to arterial ischæmia. In the acute cerebral form of plumbism the borders of the disc are swollen, ill-defined, and irregular; the disc itself is hyperæmic and mottled; the vessels are obscured, or, if observable, they are narrowed, and have delicate white lines running along their border; the veins are distended, and occasionally hæmorrhages are seen just at the border of the disc or in the retina. This form of neuro-retinitis is generally associated with eclamptic seizures, and is usually followed by optic atrophy. It is a sign of acute plumbism rather than of the chronic forms of the disease. It may occur in young women who have only worked for a few weeks or months in a lead factory. Whether vision be regained, or permanently lost, albumin may never be present in the urine. The malady differs, therefore, from the neuro-retinitis met with in chronic kidney disease. De Schweinitz and others are of the same opinion.

Instead of regarding optic neuritis as in any way specially related to and caused by saturnine poisoning, it has been attributed to deranged menstruation; to uræmia; or to lead acting mechanically, and inducing rapid effusion into the ventricles and subarachnoid spaces, the sheath of the optic nerve becoming thereby distended. Amenorrhœa can play but a minor part in its causation, for the optic neuritis occurs also in cases attended with menorrhagia. It may be a descending neuritis, or be due to distension of the sheath of the nerve. It is invariably met with in acute lead encephalopathy when there are signs of increased intracranial pressure, the convolutions of the brain being found flattened post-mortem. Lead itself may not be without some direct malign influence upon the disc and retina. Leuber and Deutschmann have suggested that optic neuritis may be caused by irritating or infective particles carried by the subarachnoid fluid from the cavities of the brain to the vaginal sheath of the optic nerves. Many such adverse circumstances may concur to produce it; but the two that play the most important part are the direct or indirect action of lead salts upon the disc and retina, and the effect of increased intracranial pressure; for in fatal cases the brain is frequently found dry and firm, extremely pale, and the arteries contracted. The movements of the iris vary with the condition of the optic nerve and retina. When there is neuro-retinitis it is dilated.

Parelle draws attention to a very interesting sequel of lead poisoning. In fifteen cases of plumbism Tancquerel noticed embarrassment of speech, but he did not correlate them with general paralysis: it was left for Delasiuve to demonstrate this. The affection apparently occurs with considerable frequency in France, and although it is met with principally amongst white-lead workers other persons do not escape. Contrary to what takes place in alcoholic pseudo-general-paralysis, the influence of heredity is not observed in saturnine cases; nor is the affection met with in women. Forty to fifty years of age appears to be the most susceptible period. *Saturnine pseudo-general-paralysis*, though aggravated by alcoholic habits, occurs in those who are temperate, and must therefore be regarded as the result of lead toxæmia. It differs from ordinary general paralysis in its sudden onset. Violent delirium is frequently its first symptom; or there may be an epileptiform seizure, nightmare, or hallucinations. These latter, whilst pretty constant in saturnine general paralysis, are very rare in the ordinary form. In other words, in addition to the usual encephalopathic symptoms due to lead, there are nightmare, hallucinations of sight, imaginary terrors, and confused ideas of being pursued or of being poisoned, just as in delirium tremens. Occasionally the approach of the disease is less characteristic, and is slowly progressive. The patients steal like ordinary general paralytics, and they have grand ideas. The later features are muscular weakness, embarrassment of speech, weakness of the intellectual faculties and of the memory. The patients sleep badly, and become excited towards evening. Following upon this comes a stage of depression, when the patients cannot stand—they are obliged to rest; some are completely paraplegic, others hemiplegic and covered with sores. Trembling of lips and tongue, and sometimes, too, of the arms and legs, are very pronounced. Speech is generally most embarrassed at the beginning, and, if anything, it is apt to be more pronounced in saturnine than in ordinary general paralysis. The loss of memory is complete; and the general hebetude of the intellectual faculties is so noticeable that the patient, even in the early period, resembles a general paralytic in the last stage of his illness.

One point of difference between saturnine general paralysis and the ordinary form is the tendency to amelioration in the former. Even after the third stage has been reached, and there have been epileptiform seizures, ideation may return, the paralysis diminish, the power of walking improve, speech become more distinct, and the patient become more intelligible. Concurrently with this improvement, however, he becomes extremely irritable on provocation.

Early withdrawal of the patient from the influence of lead may be followed by convalescence in from six to twelve months. The disease tends to cure itself; but in some cases, and without any explanation, there is a downward course, the fatal termination being precipitated by an apoplectiform or epileptiform attack. If a patient poisoned by lead subsequently falls into general paralysis it does not follow that it is saturnine; but when in a general paralytic we have a history of plumbism, this is a point in favour of the case being one of pseudo-general-paralysis. The mode of onset of the two diseases is, indeed, slightly different. The brusque inception suggests pseudo-general-paralysis. Epileptiform seizures belong rather to the early stage of this disease. There is not the permanent inequality of the pupils, and the trembling is more widely distributed in pseudo-general-paralysis than in the ordinary form. Besides being more generalised the tremor is also more intermittent, more pronounced, more spasmodic; and it appears first of all in the hands. The embarrassment of speech, too, is greater, particularly in the early stage. Disturbances of sensation, which are rare in true general paralysis, are frequently noticed; and usually consist in anæsthesia, especially in loss of the sensation of pain. In ordinary general paralysis the disease is slowly developed, is progressive, and tends to death; in the plumbism, on the contrary, the progress is quick, and even after serious and anxious symptoms have appeared, the symptoms may improve and health be slowly regained. Only a few cases have ended fatally, and in these the post-mortem appearances were those of ordinary general paralysis; on chemical analysis, however, lead was found in the brain.

In another group of cases symptoms of muscular incoördination may suggest a *pseudo-tabes* due to lead poisoning. Putnam has met with three cases, Teissier and Raymond each with one. I have also seen a similar case. In such patients there is inability to coördinate movements accurately, probably from loss of the muscular sense; in other cases there is no true incoördination, but a disordered movement due to loss of power in certain groups of muscles, the gait being that of a high-stepping horse consequent upon paralysis or weakness of the extensors of the foot, so that the toe drops when the leg is lifted, and the knee has consequently to be lifted high in order to clear the foot from the ground. In Raymond's case the symptoms appeared in a male after being exposed for only two months to lead dust; and in him the incoördination in the legs set in whilst that of the arms was disappearing. All of Putnam's cases were in women, aged respectively 15, 27, and 45 years; the muscular incoördination was aggravated by closure of the eyes. It was followed by atrophy of the muscles, impairment of vision, diplopia, girdle sensation, loss of the muscular sense, exaggerated knee-jerks, incontinence of urine, and the presence of lead therein. The point specially noteworthy in these cases of pseudo-tabes, as in saturnine pseudo-general-paralysis, is the rapid improvement under treatment; so much so as to suggest a functional and not an organic disease. Most of the symptoms have been explained by a supposed peripheral lesion; and it is said that if myelitic changes exist they are not progressive: but in a case reported by Morris of Charlestown, in which there were the symptoms of saturnine pseudo-tabes with exaggerated knee-jerks, there was degeneration of the posterior and lateral columns of the spinal cord. It is cases such as these and pseudo-general-paralysis that oblige us at this point to remark that in many cases of saturnine peripheral neuritis the lesion is not entirely peripheral but central, or a combination of both. The changes in the nerve-centres may be so slight, or so purely dynamic, that toxic conditions of blood, deranging the nutrition of ganglion cells in the spinal cord, would produce such symptoms indirectly by affecting the peripheral nerves far removed from these cells. Owing to its distance from these central cells which superintend its nutrition, the peripheral portion of the nervous system is necessarily the more vulnerable. Nutritional changes affecting the ganglion cells in the cord influence the peripheral terminations of the nerves; and changes affecting the periphery are known to influence the central cells. It is true that anatomical changes are conversely indicated in the peripheral nerves, but they are detected rather by the greater readiness with which they respond to microscopical staining reagents. Dynamic conditions may affect central cells in such a manner that we cannot demonstrate them—a statement not only applicable to the spinal cord, but to the brain in lead encephalopathy. In Minakow's, Oëller's and Drummond's cases pathological changes were found in the anterior cornua of the gray matter of the spinal cord (28). Before returning an answer to the question whether in lead paralysis the lesion is peripheral or central, let us then accumulate facts bearing upon this subject from the experimental as well as the clinical side.

In feeding animals with lead salts effects are produced with varying rapidity. On absorption of the lead there occur loss of appetite, a peculiar nervousness, constipation or diarrhœa with dark stools, albuminuria and rapid emaciation; death generally ensues when one-third of the body-weight has been lost. Many female rabbits thus treated died, and on chemical examination we found lead in the fœtuses. The tendency for animals to become pregnant is diminished, and in my own cases the male rabbits seemed to lose all sexual desire. Most of the animals were paralysed first in the hind legs, so that in walking they dragged the limbs, or they progressed with a peculiar skipping movement: subsequently the fore limbs became paralysed and the animals died in convulsions. At the post-mortem the lungs were found congested, and the kidneys also; but the peculiar feature of all cases of acute lead poisoning —in human beings as well as the lower animals—is the extreme rapidity of decomposition, and the very strong odour that is generated thereby.

A few hours after death the corpse is already putrid. The readiness with which paralysis is produced in the hind limbs of animals gives us the opportunity of studying the effects of lead upon the various organs and peripheral nerves. Déjerine maintains that there is a combined lesion of anterior roots and spinal horns, with peripheral neuritis; whilst Gombault and Charcot attribute the disordered motion and sensation to a special form of peripheral neuritis; the neuritis being segmentary and periaxial, and therefore distinct from the Wallerian form of degeneration consequent upon section of the nerve. In periaxial neuritis the axis cylinder is spared; the alteration is confined to several of the annular segments of Ranvier, whilst above and below these the nerve-fibre is normal. The lesion differs, therefore, from that met with in Wallerian degeneration, in which when the fibre is altered in its course the change extends to its remotest part. It is owing to the maintenance of the integrity of the axis cylinder that the morbid state may be remediable; sometimes, however, even in periaxial neuritis, the axis cylinder becomes fragmented, and then there occurs a peculiar modification of Wallerian degeneration, which still may be followed by a regeneration of the nerve throughout its entirety. However, Gombault's views have been combated by Pitres, who does not believe in the integrity of the axis cylinder in periaxial neuritis. These segmentary neurites are found in a large number of infective and toxic diseases; and the frequency with which Brissaud has found them in tubercular and cancerous patients, in old people, and in peritonitis, throws some doubt upon the interpretation of them in lead poisoning. It is a question whether we can regard them as true neuritis, or simply as a myelino-neuritis such as is met with in disseminated sclerosis. That saturnine periaxial neuritis occurs there is little doubt, and as little of the tendency for the nerves to be regenerated; for thus we must explain the rapid and spontaneous cure of the paralysis which takes place within two or three weeks on suspending the poison, and the fact, too, that the paralysis may be very slight.

Most neurologists insist that the lesion in lead poisoning is peripheral; and in chronic cases of wrist-drop the peripheral nerves are certainly the seat of well-marked interstitial neuritis; but are the anterior horns of gray matter in the spinal cord quite healthy? Déjerine found changes in the anterior roots corresponding to those in the altered peripheral nerves, and so did Vulpian; and we must remember that in acute lead poisoning in man or animals, when the onset of paralysis has been rapid, the most careful microscopical examination may fail to detect pathological change in the nerves.

As the electrical condition of paralysed muscles will be dealt with under article "Peripheral Neuritis," it is sufficient here to state that in lead palsy there is marked loss of faradaic excitability; whilst there may be normal or exaggerated response to galvanism if the paralysis be not of long standing. Occasionally in plumbic paralysis a small indolent swelling on the back of the wrist is noticed; it was first described by Gubler, and it conveys the impression of thickening of the extensor tendons.

Considering its frequency plumbism is not a frequent cause of *insanity*; nor does mental derangement occur without some premonition. Now and again a case is met with presenting symptoms akin to hysteria or alcoholic intoxication, which is followed by convulsions, coma, and death; but in others symptoms of melancholia advance slowly, or there is acute delirium accompanied by hallucinations, with or without affection of speech, which tends to be remittent, and to recur at night. Occasionally the delirium like that of acute mania develops suddenly, the only complaint having been headache. It is of a noisy character, and so violent is the patient that it may be necessary to restrain him. In the intervals consciousness may be regained. The patient may be blind, the urine quite free from albumin, and the temperature rather below than above the normal. As the paroxysms keep recurring with increasing severity, the medicinal means adopted to restore quietude and induce sleep—for example, bromides, morphia, chloral, or hyoscine—unfortunately tend only to precipitate the sufferer into deep coma, from which he never rallies; death being preceded by a rapid rise of the temperature. Cases of monomania have been recorded. When mental symptoms arise in plumbism, setting aside acute encephalopathy, they have usually been part of a series resembling general paralysis, such as we have described.

In deaths from plumbism lead is generally found in the internal organs. In my own cases Professor Bedson found the largest quantity of lead in the liver, and next to it in the nervous system. Gusserow found most in the muscles. It is found in the bones, in the kidneys, in the testicles, in the fœtuses of lead-poisoned animals, and in ovarian tumours. Bedson examined the breast milk of a nursing white-lead worker under my care, but failed to find lead in it. Dr. Honeyburne of Bradford has shown that in plumbism an increased amount of iron is deposited in the liver, an interesting observation when viewed in connection with the anæmia of saturnine poisoning.

What is the relation of saturnine poisoning to *abortion?* Does lead actually pass through the placenta? That it does so seems proved by the fact of its presence in the fœtus. Porak has experimentally demonstrated the passage of arsenic, copper, lead, mercury, and phosphorus through the placenta. In toxicological autopsies the possibility of such poisons having traversed the placenta should be borne in mind. Porak found that lead is very poisonous to guinea-pigs, but that abortion in them is less frequent than in other animals; although death of the fœtus is very apt to occur. It happened thrice out of six experiments. In other animals still-birth was a constant feature, and post-mortem there were found dropsy of the ventricles of the brain, and thickening and slaty discoloration of the ependyma of the third and fourth and lateral ventricles. This cerebral lesion and the chemical presence of lead in the central nervous system explain the paralytic phenomena observed in fœtuses at the time of their birth, and the convulsions and early death of the children of lead workers. Rennert has clinically confirmed Porak's observations. He found the children of potters suffering from plumbism to be hydrocephalic, and that they died within a few days after birth from convulsions. This is my own experience. Lead passes readily through the placenta, and diffuses itself through the fœtus, being found in the liver, in the nervous system, and in the skin. It is eliminated slowly by the fœtus. We found 0·1 milligramme in the liquor amnii, and in five fœtuses there was 0·09 milligramme of lead in each. The blood also contained a trace. The placenta has apparently little power in fixing lead. The accidents observed in saturnine intoxication in the newly-born depend apparently for two reasons upon accumulation of the poison in the central nervous system: first, there is dropsy, with thickening of the ependyma of the ventricles of the brain; and, secondly, when born alive the fœtuses soon die, paralytic, probably from fixation of the poison in the brain. It has been stated that lead is only eliminated by the kidneys when the urine is albuminous. This is incorrect: we frequently found traces of lead in the non-albuminous urines of female patients. In the bile fairly large quantities of lead may be found. Saliva also may contain it; we found it in sweat, but not in the mammary secretion. It has recently been shown that the principal mode of elimination of lead from the system is by the fæces. Dr. Dixon Mann, in a series of carefully-conducted analyses of the urine and fæces, both in chronic plumbism and in patients to whom a few doses only of lead acetate had been given, has not only demonstrated that by far the largest quantity of lead leaves the system by the stools, but that in certain cases its presence can be demonstrated in the fæces when the urine does not contain a trace of the metal

It is said that iodide of potassium favours the elimination of lead from the system, but the increase is hardly perceptible. In plumbism there is defective elimination both of urea and of uric acid. Retention of uric acid in the system is regarded as the cause of *gout* in plumbism, owing—as Garrod, Ralfe, Haig, and others maintain—to lead diminishing the alkalinity of the blood, lessening the solubility of uric acid, and thereby hindering its excretion by the urine. Sir Wm. Roberts questions the direct determination of gout by lead; he believes that both the gouty diathesis and lead poisoning have the same tendency (for which he has coined the term "uratosis") to precipitate crystalline urates in the tissues or fluids of the body. This saturnine uratosis, he maintains, is simply reinforced by a previously existing gouty tendency. In the North of England we seldom meet with gout and plumbism, and in the few cases in which I have observed it there has been a strong hereditary disposition to gout. In several cases the elimination of lead by the kidneys seemed to be inversely proportional to that of uric acid. That lead does favour the retention of uric acid in the system is probable; and from the readiness with which gouty seizures in the London hospitals have followed the administration of small doses of plumbic acetate, gout and plumbism seem at first sight to be causally related to each other. I am not alone in maintaining that the relationship of the two is not immediate or direct. Professor Ebstein of Gottingen says, "I have come to the conclusion, on the testimony of doctors to the lead works on the Upper Hartz Mountains, where gout is of relatively frequent occurrence, that with gouty individuals lead poisoning strongly predisposes to a gouty seizure." Ebstein's opinion confirms Roberts' and my own. During the years 1878-85, in the lead works of the Upper Hartz Mountains, 1103 cases of plumbism came under observation; of which 103, or 9·3 per cent, presented signs of gout. It is difficult to explain why the association of plumbism and gout should be so frequently observed in London and so seldom in Newcastle, Edinburgh, and on the Hartz Mountains. It is probable that the explanation is to be found in the difference in the food, external circumstances, and hygienic precautions, and in the habits of the people as regards the use of stimulants, beer disposing to uratosis more than whisky. The fact remains that in those districts where gout is infrequent the disease is not promoted by chronic lead poisoning; but where gout prevails even small doses of lead seem sufficient to produce gouty symptoms.

During lead colic the urine and urea are diminished; but the crisis once over, they gradually rise to near the normal. Vomiting, diarrhœa induced by aperients, and the absence of food, doubtless favour this deficiency. The total nitrogen eliminated was found by Surmont and Brunelle to be diminished during colic. In my own cases the urea was only a half or a third of the normal. Potain states that the liver is diminished in size during colic; but this is doubtful, as at this particular time, owing to the retraction of the abdomen, the liver ascends under the costal arch, becomes less oblique, and diminished in its vertical diameter. Hepatic function is deranged, for pathological urobilin may be found in the urine. The glycogenic function is particularly disturbed during colic, as the administration of syrup is said to be followed by glycosuria; but in my own experiments upon rabbits the liver always contained glycogen.

As regards the elimination of uric acid in plumbism there is considerable difference of opinion. Garrod maintains that it is diminished during the attack. Surmont and Brunelle found it diminished in four out of eleven cases, after colic increased; the increase or diminution of the uric acid was in no way proportional to the severity of the colic, and old saturnine patients tended to pass it in excess. In my own clinical experience the amount of uric acid has varied; it has sometimes risen as high as 12, 16, and 21 grains per diem; the normal being 0·5 gramme to 1 gramme, or 7 to 15 grains, whilst the lowest was 0·13 gramme or 2 grains. In the latter case the urea also was frequently much below the normal; and it is an interesting point that on the days the patient passed the largest quantities of urea she was free from headache. The urine generally contained a trace of lead. The elimination of lead and of uric acid may be inversely related to each other; as if the presence of the metal in the blood favoured the retention of uric acid in the system. Surmont and Brunelle found the amount of creatin and hippuric acid increased, an interesting point, seeing that the total nitrogen and urea are diminished; it indicates how profoundly metabolism is affected in saturnine poisoning. Goetze of Wurzburg maintains that in the arthritic attacks and colic uric acid keeps below the normal, and remains low for some time after the attack. During chronic plumbism it fluctuates within the limits of the normal. He also found that in the acute attacks chlorides were thrown off in small quantity, and increased subsequently. Of the elimination of phosphoric acid by the kidneys not much is known. Taking 30 to 50 grains of phosphoric anhydride as the daily average in health, I found that it varied from 25 to 77 grains. Goetze found it always low in chronic plumbism. Some writers have alluded to the presence of hæmatoporphyrin in the urine after lead colic.

The *morbid anatomy* of acute plumbism is practically nil. In lead encephalopathy the brain may be shrunken and dry; it may appear as if it had been compressed, all the blood-vessels being constricted. The brain substance may be pale and extremely firm, or pale and œdematous as in cases of uræmia. The small intestine may be extremely contracted in places. The kidneys are generally stated to be atrophic and the seat of interstitial nephritis, but this is principally found in the chronic cases. In acute lead poisoning, both in man and animals, the epithelium of the convoluted tubules is enlarged, and the protoplasm is the seat of cloudy swelling, becoming fatty, granular, and rapidly breaking down; the débris of it may be seen in the interior of the tubules. The change in the kidneys is therefore parenchymatous at first, and is frequently accompanied by some degree of glomerular nephritis; for the afferent vessel to the glomerulus may be seen surrounded by numerous round cells. Bowman's capsule is thickened, and there is a multiplication of the cells that line its interior or of those that lie between the coils of the capillaries. From the external surface of the glomerulus round cells may be observed penetrating between the convoluted tubules, causing an increase of the connective tissue at this particular part of the kidney, and giving rise therefore to an interstitial nephritis secondary to the parenchymatous. In emphasising the fact of tubular nephritis being the primary lesion in lead kidney I am not ignorant of the views held by other pathologists as to the condition of the interstitial tissue; but changes therein seem rather to follow those occurring in the tubular epithelium. Ollivier mentions parenchymatous nephritis; and in the kidneys of animals experimentally treated by Charcot and Gombault there were degenerated epithelial cells in the tubuli uriniferi, with proliferation of small round cells around those tubules only whose epithelium was affected. Coën and d'Ajutolo found in rabbits, killed at varying periods after the administration of acetate of lead, that the epithelium of the urinary tubules first became swollen, then degenerated and shed; and that in the more chronic cases there was a glomerulitis followed by thickening of the vessels and interstitial nephritis. The more recent experiments of Hirsch upon guinea-pigs, detailed in his Thesis for the Doctorate in Medicine of Leipzig University, revealed extensive swelling of renal epithelia, degeneration and shedding of the same accompanied by the presence of hyaline tube-casts in site, thickening of Bowman's capsule and the presence of round cells between the tubules.

Hirsch rather regards the epithelial and interstitial change as occurring simultaneously; but as he states that epithelial degeneration constitutes a feature constantly found in all lead kidneys, and is the specific lesion caused by lead, he too is clearly of opinion that it is one of the earliest and principal effects caused by lead in these organs.

Lead acts very injuriously upon the eliminating organs. The liver, like the kidneys, is the seat of marked changes. It is in this organ that the largest amount of lead is found on chemical analysis; the liver looks fatty, and on microscopical examination the hepatic cells are observed to be atrophied and granular, or to be the seat of advanced fatty degeneration. In some cases there is intercellular cirrhosis; in others a marked increase of connective tissue between the lobules. Whatever view we take of the pathology of plumbism, it must be admitted that lead rapidly deranges metabolism. It destroys the functional activity of the liver and kidneys, slowly inducing changes within their secreting cells; and although we cannot forget that certain symptoms of encephalopathy depend upon the presence of lead in the brain, they are more probably caused by animal poisons retained within the system during inadequate hepatic and renal elimination, a proof of which auto-intoxication is that in some of my cases of fatal saturnine encephalopathy, characterised during life by convulsions and coma, not the slightest trace of lead was found in the brain after death. This opinion, fully expressed in my Goulstonian Lectures (1891), has met with considerable acceptance. In America the treatises of Hughes and Carter, and of Miller and Ring, lend the weight of their authority to it.

The *treatment* of lead poisoning is preventive and curative. Lead pipes for the conduction of drinking-water should be disused, and their place taken by pipes made of iron or glass. Lead cisterns for the storage of water for culinary purposes should not be allowed. All drinking-water should be transmitted direct from the main into the houses, and before being used in the morning the water should be run off for a few minutes at first, so as to empty the lead pipe. The addition of carbonate of lime or silica to water, provided no excess of carbonic acid be present, frequently allows of the formation of a protective covering on the interior of the pipe. The presence of micro-organisms in water increases its solvent power upon lead, owing to the influence of chemical products formed during their multiplication; hence sewage-polluted water—which also contains chlorides, nitrates, and nitrites—is especially dangerous. To stock the reservoirs with fish is an inexpensive and efficient method of reducing the plumbo-solvent action of moorland water.

As regards industrial lead poisoning the Home Office has issued regulations, the strict enforcement of which in factories has been beneficial. Men and women therein employed should be medically inspected once a week, and an increasing anæmia should be regarded as a disqualification. Frequent ablution, the wearing of overalls and respirators, and washing before eating diminish the risk to some extent; but the women are unable to take the prescribed baths at their menstrual periods. Washing the hands with water containing hypochlorite of soda or paraffin is a good preventive. Acidulated drinks, composed of water in which sulphuric acid and magnesium sulphate are dissolved, and to which lemon has been added, are provided in all white-lead factories, and the work-people are encouraged to drink freely of them; but, as I have said, the preventive power of these drinks is feeble; an excess of free sulphuric acid in the water would redissolve any sulphate of lead formed in the alimentary tract, and the tendency would be favoured by the presence of fresh lemon juice. Besides, sulphate of lead is soluble in the hydrochloric acid of the gastric juice. The alcoholic habit strongly predisposes to plumbism. Milk should form a large part of the dietary of the work-people; and no person should be allowed to work in a white-lead factory before breakfast, for clinical experience and experiment have demonstrated that the presence of food in the stomach diminishes the solvent influence of the gastric juice upon lead. The addition of a small quantity of sulphur to the milk increases its protective powers.

For the colic, if not severe, a mild purgative, such as magnesium sulphate or castor oil, may be sufficient; but, should it be accompanied by vomiting, effervescing mixtures may be tried, and enemas of warm water and olive oil resorted to. Should the abdominal pain be severe, small doses of tincture of opium or of belladonna may be added to the aperient; or a hypodermic injection of morphine and atropine may be administered, or belladonna fomentations applied. A mixture of magnesium sulphate and potassium iodide generally acts well. Occasionally it is difficult to relieve the colic, but it will generally yield to the influence of a warm bath. When the colicky pain and vomiting have been relieved, or when colic alone is present, monosulphite of soda, in five-grain doses thrice daily, has a wonderful influence in soothing the general symptoms. In a mild case abdominal pains and paralysis quickly disappear under its influence.

As an eliminant potassium iodide still finds favour, and rightly so; but in the early part of the treatment of acute plumbism it should be used with caution, for under its use lead, which has been deposited in the tissues and is therefore inert, might be redissolved, and fresh symptoms of saturnine poisoning reappear. Occasionally the drug causes albuminuria. In a female patient transferred to my care by my colleague Dr. Geo. Murray, the administration of five-grain doses of potassium iodide was followed by a rise of temperature (101·8°) and the presence of albumin in the urine. On discontinuing the medicine the temperature fell and the albuminuria disappeared, but on renewing the potassium iodide the albuminuria returned. The bromide is also efficacious. Dr. Burney Yeo quotes Semmola as having found electricity useful. The patient is placed in an acidulated bath, and one pole of the continuous current is applied to the tongue while the other remains in the water: or, without using the bath, one pole may be applied to the tongue and the other to the epigastrium. It is stated that the blue line disappeared from the gums in a few weeks, and examination of the urine showed increased elimination of lead. For saturnine paralysis, which is sometimes very obstinate, electricity and nux vomica, with potassium iodide, or the subcutaneous injection of strychnine, are useful; and for the anæmia, which remains after the painful symptoms have disappeared, tabloids of bone marrow have given encouraging results.

For lead encephalopathy, when convulsions rapidly succeed each other, the inhalation of nitrite of amyl is very serviceable. Under its influence the pulse regains its softness and recovers its frequency. As the urine is often suppressed, the subcutaneous injection of pilocarpin may be called for.

Seegelken of Jena has successfully practised tapping of the lumbar region of the spinal cord in coma of lead poisoning. The patient was a house-painter, who after suffering from lead colic was seized with recurrent convulsions and unconsciousness. The urine was non-albuminous. In the intervals between the convulsions the right arm and leg were observed to be paralysed. As coma endured for two days Seegelken had recourse to lumbar tapping. Sixty grammes (a little less than two ounces) of cerebro-spinal fluid were thus removed under a pressure of 310 millimetres, which gradually fell to 80 towards the end of the operation. Shortly after the puncture the patient gradually regained consciousness; that evening he sat up in bed, and within thirty-six hours all cerebral symptoms had disappeared. On the theory that the convulsions and coma of lead encephalopathy are due to acute œdema of the brain, it is interesting to note that the fluid as it first flowed was clear, serous, cerebro-spinal; whilst towards the end it was cloudy, a circumstance which suggested to the operator its encephalic origin.

Diagnosis.—In the stage of acute colic the extreme pain in the abdomen might be mistaken for severe intestinal cramp, but scarcely for peritonitis, as there is no rise of temperature, and the abdomen is usually retracted. No distended coils of intestine either are noticeable. The abdominal pain, though sometimes relieved, is generally increased by pressure, when it is observed to be more or less unilateral, and associated with pain along the course of vagus in neck on the same side; the pulse is small. The history of the case, the presence of a blue line on the gums, distinct cachexia, and a peculiar restlessness suggest plumbism, the diagnosis of which would be confirmed by lead being found in the urine on chemical examination. This may be done as follows. Evaporate 50 cubic centimetres or 2 ounces of urine to dryness; ignite the residue, extract the lead from this by dilute hydrochloric acid. Precipitate the lead as sulphide by means of sulphuretted hydrogen or ammonium sulphide. The objections to this procedure are its tediousness and the necessity for the preliminary destruction of organic matter. To the method for detecting lead in urine mentioned by von Jaksch in his *Klinische Diagnostik*, which Abram and Marsden of Liverpool found both accurate and simple, these objections do not apply. A strip of magnesium is placed in the fluid to be examined. Ammonium oxalate in the proportion of 1 gramme to 150 c.c. is added. If lead is present it is deposited on the magnesium. Some deposit is seen within half an hour, but it may require a longer exposure. The slip is then washed with distilled water and dried. In order to confirm the test (*a*) warm the slip with a crystal of iodine upon it; yellow iodide proves the existence of lead—the probability of its being cadmium need scarcely be entertained; (*b*) dissolve the deposit in nitric acid and apply the usual tests for lead. In making use of this method care must be taken to have the surface of the magnesium bright and free from the presence of any oxide. This is an extremely delicate test, capable of detecting 1 part of lead in 50,000, whether the metal be dissolved in water or contained in an organic liquid like urine.

Bilateral paralysis suggests a toxic cause. Usually but not always both wrists are affected in lead poisoning. The fact of the muscles of the upper extremity being affected, particularly the extensors of the wrists and fingers rather than those of the lower limb, is suggestive of saturnine as against arsenical and alcoholic paralysis. Although not wholly absent, there is, generally speaking, less tenderness on grasping the muscles in lead than in either alcoholic or arsenical paralysis; whilst if anything there are more rapid atrophy and greater sensory disturbance in arsenical than in saturnine poisoning. At one stage of the illness lead paralysis may resemble anterior poliomyelitis and progressive muscular atrophy; but in plumbism the paralysis is usually limited to the extensor muscles, especially those of the wrists and fingers, whereas in the spinal cord lesion both flexors and extensors are involved. Tremors may be present, but they are distinguished from the movements observed in mercurialism by being less wide in their range, usually ceasing during rest, and in their less tendency to exhibit remittency.

In lead paralytics there is usually a history of colic. The loss of power primarily affects the extensor communis digitorum, and subsequently the other muscles supplied by the musculo-spiral nerve with the exception of the supinator longus; a peculiarity which distinguishes it from a local lesion of that nerve. When the paralysis is well marked, the affected muscles fail to respond to induced electrical currents, whilst to a slowly interrupted galvanic current they usually respond freely. Dr. Buzzard, in the absence of other physical signs or a suggestive history, has found this test to be of signal service. Like myself he too has found the supinator longus occasionally affected in lead poisoning; so that the dictum of Duchenne on this particular point is scarcely correct. It was Remak's observation that the cells in the anterior horns of the gray matter of the spinal cord represented muscles that are functionally associated; hence when the supinator longus was affected the brachialis anticus and biceps were at the same time involved, thus forming the "forearm type" of lead palsy. Ferrier and Yeo, by irritating the brachial plexus of the monkey, have experimentally demonstrated that each motor root represents rather a distinct functional combination than contiguity in peripheral nerve distribution; and that the movement of supination is subserved by roots coming from a part of the cervical enlargement higher up than that which brings about extension of the wrists. Thus physiologists seek to explain the frequency with which the supinator longus escapes in lead poisoning, whilst other muscles supplied by the musculo-spiral nerve are affected.

Prognosis.—The prognosis is favourable in the stage of colic and vomiting. Very few cases of plumbism end in death at this particular period of the illness. When, however, the attacks of colic are renewed from time to time, and recur over a long period in patients whose health is deteriorated, and in whose urine there is albumin, the illness must naturally be regarded as grave. Under electrical and medicinal treatment, uncomplicated saturnine paralysis generally disappears; but in some cases the recovery is extremely slow and at the best is incomplete, for weakness of the wrists endures a considerable time. The prognosis of acute lead encephalopathy with convulsions is extremely grave. Not only is there danger of the patient dying in the seizure without regaining consciousness, but should the symptoms subside, the mental condition for some time afterwards may remain unhinged, speech and memory may be defective, or there may be permanent blindness, and this is the most common sequel.

ARSENIC.—Of the cases of criminal poisoning in this country those by arsenic form the largest number; accidental poisoning by arsenic forms the smallest. In the five years ending 1890, seventeen persons died from taking arsenic—twelve males and five females. The comparative tastelessness of the drug is one reason why it is so frequently resorted to for criminal purposes. The metal itself is innocuous; but when acted upon by the juices of the animal body, or when volatilised and transformed into arsenious acid, it assumes highly poisonous qualities. Its effects are deleterious whether it be respired as dust, swallowed in a soluble form, or applied externally to the skin. Its escharotic properties have long been known. In miners employed in the extraction of arseniferous metals a form of pneumonia, which rapidly becomes purulent, has been observed; ulceration of the skin and mucous membranes is also met with. Many of the symptoms complained of by zinc-smelters are due to the presence of arsenic in the fumes. Of the miners of Schneeberg in Saxony, who extract cobalt—a mineral composed mostly of nickel and bismuth—3 per cent die annually from a disease locally known as "cancer of the lung," a chronic affection probably due to the presence of arsenic in the cobalt; and in our own country the men who are engaged in colour works, where emerald green, a mixture of arsenic and copper, is made in large quantities, occasionally suffer from sores of the skin—particularly in the axilla and groin, along the sides of the nails, and on the penis. These are caused by the dry dust which settles upon the skin and erodes it; the evil is aggravated by friction of the clothes, by the presence of perspiration, or by handling of the genital organs during micturition with fingers covered with the green dust. Ulcers on the penis of workmen engaged in making emerald green have been wrongly attributed by their wives to other causes. In this country the dangers consequent upon the manufacture of arsenic have been much diminished by improved ventilation, the use of a fan, and by what is technically known as the "wet method." I have visited the emerald green manufactories in England and examined many of the workmen; and although I admit that skin eruptions and ulcers still occur, they do so far less than the public have been led to suppose. Men and girls who are employed in the making of artificial flowers, or of toys dusted with Scheele's green mixed with other pigments—with chromate of lead, for example—suffer from diffuse erythema, minute vesicular eruptions becoming pustular, ulceration, and gangrene of the skin. The eruptions are noticed mostly at the bends of the fingers, elbows, and arms, the angles of the nose and lips, the inside of the thighs, and between the toes. Several of the bright red colours used as pigments in the arts and commerce contain arsenic; for example, cochineal red, Persian red, vermilionette, and rosaniline. The use of arseniates as mordants in the dyeing of fabrics such as "opal blue," and their reckless employment in the colouring of confectionery, have caused many fatal accidents.

The occupation of rooms lined with wall papers containing arsenic has frequently been followed by a series of symptoms, the real nature of which was long unrecognised. In 1839 Gmelin called attention to the danger, and Kramer in 1852 instituted experiments to determine whether a volatile arsenical compound could be liberated under the circumstances; but it was reserved for Halley in 1858 to record the first fatal case of poisoning attributable to this source. Of the pigment present in the wall paper as much as 59 per cent was arsenite of copper. Besides the arsenical dust that falls from these wall papers it is maintained that arseniuretted hydrogen or arsine is evolved—a gas which arises from the contact of arsenious acid with organic matter, the long-continued inhalation of which is dangerous. Removal of the patient from such a room is generally sufficient to effect a cure. Considerable doubt has been expressed in regard to poisoning from arsenicated wall papers, and numerous experiments have been undertaken to solve the question. The symptoms have been attributed to the absorption of dust, to the inhalation of arsenical gas, or to the combined action of the two factors; but lately improved bacteriological methods in the hands of Selmi, Hamberg, Gosio, and Sanger have demonstrated that a volatile arsenical compound is formed by the action of certain moulds on organic matter containing arsenic (86). Taking potato pulp containing 0·5 to 1 per cent of arsenious oxide, and exposing it to the air of a cellar, Gosio found an abundance of mould upon it in a few days, and an intense garlic odour was emitted. Pure cultures were made from this growth on sterilised arsenical preparations; but the peculiar odour was only noticed from such organisms as the Aspergillum glaucum and Mucor mucedo. On decaying paper Saccardo found the Penicillium brevicaule, a mould so peculiarly sensitive to arsenic that Gosio has proposed to utilise it as a means of testing for arsenic in toxicological work. All micro-organisms may have a slight action in the course of time; but there are a few arsenio-bacteria whose operation is immediate and intense. Of these Penicillium brevicaule stands out as the most sensitive, and it can be employed for the detection of arsenic in the presence of large amounts of organic matter. By this interesting and extremely delicate micro-biological method one part of sodic arsenite in 1,000,000 may be detected in a milk culture. In confirmation of Gosio's opinion Sanger's experiments show that a gaseous or volatile compound is generated from decaying arsenical matter, with which the air of a room may be charged. The volatile compound formed is not exactly known. The chances are that it is not arseniuretted hydrogen, but a neutral organic derivative of arsenic. In the presence of oxygen these compounds are most largely developed in combinations of carbohydrates with arsenious or arsenic acid or their salts; and the conditions favourable to their development by moulds are moisture, a temperature ranging from 15° to 35° C. (60°-95° F.), and a liberal supply of oxygen. This formation of volatile compounds explains those cases of poisoning where an arsenical wall paper underlies another paper free from the metal; and also the fact that, whilst the effect of an arsenical paper may be diminished by varnish or size, the danger is not altogether removed. In Germany the manufacture of wall papers containing arsenic has long since been interdicted.

Arsenical poisoning has frequently followed the application of quack ointments to the skin for cancer; and the liquid in which fly-papers have been soaked has been used for criminal poisoning — the active principle of the brown *papier moure* being arsenious acid. Serious consequences have also followed the wearing of garments or gloves dyed with arsenical green. Fowler's solution contains 4 grains of arsenious acid to the ounce, and is an excellent remedy for chorea. It should be carefully administered, however; for when given in rather large doses, or for too long a time, it has frequently caused peripheral paralysis, bronzing of the skin, and ulceration of the intestine. Arsenious acid is largely employed by dentists to destroy the nerve in decayed teeth, and hitherto no serious accident has arisen; but its employment is not wholly free from risk, seeing that the quantity used is never weighed by the dentist; however, the quantity placed in the tooth cavity is usually very small, probably not more than $\frac{1}{20}$ grain. Arsenic, we know, does not form an albuminate; thus it is that it forms such an excellent paste for dental purposes; it can penetrate into all the recesses of a carious tooth. Plants soon wither if placed in a solution of arsenious acid; and if they have been grown on soils containing small quantities of arsenious acid infinitesimal traces of the metal may be found in their tissues.

Certain animals, such as partridges, are said to be refractory to arsenic. We do not know whether or how far the eating of the flesh of animals that have ingested arsenic may be followed by ill effects in man. The risk would be less in eating the flesh than the internal organs. Strychnia has been found in the muscles of fowls. The "aqua tofana," once renowned as the means adopted by a secret society of women for the wholesale poisoning of married men, was made by rubbing white arsenic into pork, exposing it to the sun for several days, and collecting the liquor as it drained away. This fluid is not only extremely poisonous, but is also said to defy chemical detection. Its virulence probably depends upon a mixture of arsenites of cadaverine, putrescine, and other unknown ptomaines.

Arsenious acid is a strong poison to nearly all forms of animal life—from the highest to the lowest; the symptoms vary according to whether the poison has been inhaled as vapour, drunk in a soluble form, or applied externally; the condition of the health and the habit of the individual at the time are not without their influence. Von Tschudi, in 1851, drew attention to the practice of arsenic-eating by the mountaineers of Styria, Hungary, and certain parts of the Punjab; the belief in these districts being that under the influence of the drug the respiratory power is increased, and the complexion, particularly of the women, improved. We are familiar with its beneficial influence in certain forms of skin disease and in asthma; and although it is maintained that the Styrian peasantry, beginning the practice with small doses, gradually increase it to 30 grains, considerable doubt has been expressed concerning the practice; especially as we are told that the people who thus indulge live to a great age. Certainly a tolerance to the drug can be established. Half a grain of arsenious acid, for example, is a dangerous dose to give to a dog; yet a mongrel Scotch terrier of my own took more than a grain of arsenious acid daily for several months. Under its employment in smaller doses an intense stimulus was given to nutrition. The animal gained considerably in weight, became sleek and well covered, and the hair of its coat, which was thick, coarse, and stumpy, became long and silken. All who saw the dog were struck by the improvement in its appearance, particularly as regards its pelt. Arsenic has long been given by grooms to horses with their food to improve the coat and render them plump and well conditioned. Once begun, however, the practice has to be continued; otherwise the animal shows signs of falling off. If this be true as regards animals, it has been stated that in man no such tolerance of the drug is established, and that the stories of the Styrian arsenic-eaters are purely imaginary. Tschudi's statements have been severely questioned (7). Dr. Parker of Nova Scotia (71) reports the death of a male arsenic-eater who had taken from 2 to 3 grains of the drug daily for five months in the hope of relieving a dyspepsia. When he discontinued it he found he was not so well. He stated that the skin was not improved by it, and that it had no appreciable effect upon the respiratory organs, nor upon the muscular system, which remained well developed; but he thought that the genital organs were stimulated by it. However, symptoms pointing to an extremely irritable state of the gastro-intestinal tract set in, followed by thirst, suppression of urine, collapse and death. In this case the daily use of the drug did not beget any enormous tolerance of it in the economy—a circumstance quite in keeping with the opinion of Christison, that whilst the system may become habituated to the use of some of the organic poisons, habit does not diminish, but increases the activity of inorganic poisons entering the blood. The publication of Parker's case drew from Dr. Craig Maclagan of Edinburgh (in the same journal a month later) a paper giving an account of his travels through Styria, and of his personal observation of the practice of eating a mineral substance "Huttereich," known to be arsenic, which was locally asserted to render respiration easy during mountain-climbing, and to act as a condiment and tonic; its more immediate effect on the system is to make the people lively, combative and salacious, to which latter circumstance was attributed "the inordinate number of illegitimate children in some of these places, the proportion sometimes rising nearly as high as 60 per cent of the total births." Maclagan was an eye-witness of the practice of arsenic-eating in the case of two men, one aged twenty-six and the other forty-six years of age. To one of these men 6 grains were given on a piece of bread. This was swallowed, for the mouth was carefully examined afterwards and found quite clear. No immediate effects followed, but on examination of the urine arsenic was found therein. Whilst admitting that arsenic-eating is not in any sense of the word a universal habit amongst the Styrian peasantry, or even freely indulged in by the male population, Maclagan maintains "that decisive evidence has been brought forward not only to prove that arsenic is well known and widely distributed in Styria, but that it is likewise regularly eaten in quantities usually considered sufficient to cause immediate death." In 1875 Maclagan published a second paper describing, on the authority of Dr. Knapp, a public exhibition of arsenic-eating by two men, and mentioning that other cases were known to him. Knapp is of opinion that only strong persons can indulge in the practice, but that these attain great age; that the virtues claimed for arsenic exist; that the drug is taken at intervals of a few days, and that there is no longer any doubt about the arsenic-eating in Styria. A Royal Commission has reported that although the practice exists it has been grossly exaggerated.

I have been directly informed by Dr. Eberstaller, the town's physician of Gratz, that the practice of arsenic-eating was unknown to him, but that Dr. Marik, in a paper read before the Styrian Medical Society (57), had revived professional interest in this important matter by bringing to light eight cases of arsenic or *nidri* eating—four in Deutsch-Landsberg, two in Oberwölz, two in Vorau, and one in Ligist. Moreover it was stated that there were two arsenic-eaters at Houtberg, and one each at Grafenberg and Raindorf. Of the eight cases one was a man aged sixty-six, who began eating arsenic at the age of thirty, and whose father—also an arsenic-eater—had died at the age of seventy-seven. In the presence of Drs. Knapp and Buchner this man took 2·16 grains of orpiment (arsenic trisulphide), and stated that he became an arsenic-eater at first under the belief that the drug was a prophylactic against typhus fever. Beyond an indisposition of two days' duration he had never been ill these thirty-six years. When feeling lazy and disinclined to work he would take a small quantity of arsenic, and in a few hours would feel invigorated, and fit for a long pedestrian journey. He maintained that sexual potency is rather increased by it than otherwise, and that after taking arsenic he must eat some food. The other seven arsenic-eaters were reported to be strong healthy men, who have indulged in the drug for periods varying from eight to twenty years. In the urine of four of these persons Buchner proved the presence of arsenic, both qualitatively and quantitatively; in one instance 0·385 grain being found.

Marik therefore maintains that arsenic-eating is still practised in the north and north-western parts of Styria; and that, according to Schäfer, the practice is not unknown to peasantry of the districts of Hartberg, Lamprecht, Leoben, and Oberzeiring. It is difficult to obtain accurate information as to the number of arsenic-eaters in Styria, for the people know that the practice is illegal, and the greatest possible secrecy is observed. The practice has by no means died out, and the reasons assigned for taking the drug are still the same as they were many years ago; namely, that it gives strength and vigour to the muscular system, increases the respiratory power, aids digestion, and is a prophylactic against infectious fevers. Believing that it acts as a cosmetic, it was used by young ladies in the upper classes of society in Florence some years ago.

Symptoms.—When administered in small doses arsenic acts as a tonic by gently irritating the stomach; thereby provoking appetite. It exercises a distinct influence upon nutrition, improving muscular tone and creating fresh vigour.

Poisoning by arsenic may be acute or chronic. Arsenic—white arsenic or arsenious acid—is soluble in water, has a faint sweetish taste, and on volatilising it emits a strong garlicky odour. It is an escharotic when applied to any surface in a concentrated form, and an irritant even when diluted. From a quarter to half an hour after taking a large dose a burning pain is felt in the œsophagus and stomach, which spreads over the whole abdomen, and is accompanied by a sense of constriction at the throat and a metallic taste in the mouth. Consequent upon the intense intestinal hyperæmia are violent purging and vomiting; the discharges, at first mucous, become bilious and tinged with blood as in English cholera. Thirst becomes excessive, the urine is suppressed, arterial tension falls, and the patient soon becomes collapsed and his extremities cold; owing to the abdominal tenderness the respiration is laboured and embarrassed. Gradually, however, the pale face becomes cyanosed, cramps keep recurring, the temperature falls, convulsions or coma supervene, and death follows in from five to twenty hours. There is a close resemblance between such a case and cholera; and were the latter epidemic at the time, and nothing present in the circumstances to excite suspicion, such a case, even in the hands of an experienced physician, might be mistaken. In some cases there is only a profuse watery intestinal discharge; and whilst during life the case closely resembles cholera, the suspicion is not dispelled by the appearances presented at the autopsy.

A more common form of poisoning is the subacute. The symptoms of slow arsenical poisoning are of a milder character, and are remittent. The vomiting and purging may intermit, and the abdominal pain may subside, although it is still present on pressure. The other characteristic symptoms are persistent thirst and painful deglutition; scanty urine, red in colour, and frequently albuminous; heart weak and irregular; abdomen tumid; face cyanosed; skin cold and clammy, and exhaling the peculiar odour of arseniuretted hydrogen; the legs drawn by cramps and convulsions, whilst the mind, as a rule, remains perfectly clear. From time to time there is a remission of the symptoms, the patient rallies, and there is hope of recovery; but the improvement is not maintained, the symptoms recur, and death ends the scene.

A single large dose of arsenic may prove quickly fatal; or it may cause a prolonged illness ending fatally. If not followed by death convalescence is slow, and is apt to be retarded by various disorders, principally arising from the alimentary canal; or nervous symptoms connected with motion and sensation may appear, such as anæsthesia, hyperæsthesia, loss of the thermic sense, and paralysis. Joubert-Gourbeyre collected 100 cases of arsenical poisoning, and in more than one-half all the extremities were affected; one-fourth were paraplegic, in the remainder there was hemiplegia or some limited form of paralysis. The loss of power was mostly limited to parts below the knee and elbow. Arsenical paralysis, like that due to alcohol, usually begins in the legs. On the occurrence of paralysis the muscles undergo rapid atrophy, are usually sensitive to pressure, and at an early date present the "reactions of degeneration." These symptoms are usually met with when arsenic has been taken for a long period; but Meirowitz reports the case of a young man aged nineteen, who inadvertently swallowed 5 grammes (77 grains) of arsenious acid. This was followed by extremely severe symptoms of acute arsenical poisoning; they subsided, and in three weeks afterwards his legs became painful and his feet swollen, which symptoms gradually increased until he was unable to walk without crutches. Subsequently his gait became ataxic, and his feet cyanosed and cold; the muscles of his legs atrophied rapidly, and were painful on pressure; the calf muscles were the seat of involuntary twitchings; the foot, patellar, and cremasteric reflexes were absent; the soles of the feet were anæsthetic, whilst the skin of the lower half of the legs was hyperæsthetic, with deficient response to the faradaic and galvanic currents. The hands were also affected, the movements of the fingers being greatly impaired. These symptoms of multiple neuritis occurred in the patient two months after the swallowing of a single large dose of arsenic.

Arsenical multiple neuritis in some respects resembles subacute poliomyelitis; but there is more pain, and the combination of sensory disturbance and tendency to rapid cure diminishes the resemblance. Is the lesion peripheral or central? Wood alludes to the experiments of Popoff, who found in dogs, killed in a few hours by arsenic, the spinal cord inflamed; and in cases of slower poisoning that the small blood-vessels in the cord were thickened, the protoplasm of the large multipolar cells opaque and granular, and their nucleus indistinct: subsequently the cells became vacuolated. Erlicki and Rybalkin found disease in the anterior horns of gray matter and in peripheral nerves; and they maintain that myelitis, and particularly changes affecting the multipolar cells, are consequences of arsenical poisoning. Whilst the alterations were well marked in the cord on microscopical examination, there had been no tenderness along the course of the nerves during life. As in lead poisoning, it would appear as if the lesion might be peripheral or central, or a combination of both. That the central nervous system is affected by arsenic is also maintained by Campbell, who found the nerve-cells in the cortex of the brain vacuolated, and degenerative changes in the small blood-vessels. The nucleus becomes swollen, there is loss of its reticular structure, and it stains with difficulty; granules of fat appear, these coalesce, forming oily droplets which enlarge, and ultimately coalesce, so that the whole of the nucleus becomes converted into oily material. The nuclear membrane then ruptures, allowing the contents to escape, and a non-lustrous vacuole is left.

The administration of arsenic for a long time, even in small doses, must induce changes in the nervous system. Into the nutrition of the nervous tissues arsenic must enter, deranging their function; particularly that of nerve-fibres, which appear to be more susceptible than nerve-cells. Altered function is followed by altered structure. In metallic poisoning one is struck by the bilateral symmetry of the peripheral nervous lesions, and that certain fibres, motor or sensory, are more affected than others. Again, there may be a simulation of tabes, with ataxia, muscular anæsthesia, and loss of knee-jerk, consequent upon a preponderant affection of the afferent nerves. How peculiarly susceptible nerves are to all toxic influences has been shown by Sklaret of Berlin, Ringer, and Murrell. On injecting arsenious acid or an arseniate into animals, they found that the drugs acted directly upon the nerve-centres, producing paralysis of motion with loss of sensation and reflex action, and that they were highly toxic also to the peripheral nerves.

Different organs exhibit a selective influence in regard to arsenic. In acute poisoning this is seen in the gastric mucous membrane; and in chronic forms in the liver, kidneys, and heart. The skin is affected in chronic arsenicism. In the treatment of chorea by increasing doses of Fowler's solution, whilst the disease may be cured, there is frequently left after it deep brown pigmentation of the skin, either of the face especially, or spread generally over the trunk and limbs—a pigmentation which does but deepen under the administration of potassium iodide, given in the belief of its being an eliminant for arsenic. Arsenic is said to prevent the acne of bromism; but, if this be so, yet in such patients mild pigmentation may follow—first as discrete small spots which ultimately coalesce.

Sex is not without its influence in the evolution of the symptoms. Cox investigated 1700 cases treated by arsenic and found that the gastric symptoms are commoner in women, and the intestinal in men; that the conjunctivæ are often inflamed in men, and that nervous symptoms are more frequently observed in women. Children and young people bear arsenic well; but old people are peculiarly susceptible to it, and in them signs of nerve degeneration rapidly appear.

When arsenic is administered in small doses for a long time the symptoms may be slight; the health is so gradually deteriorated that disease from other causes is simulated: in other cases the slow form of poisoning is but a repetition in miniature of the acute. There may be gradual loss of appetite, emaciation, increasing feebleness, depression of spirits, irritability of temper, sleeplessness, pigmentation of skin, conjunctivitis, catarrh of the nasal mucous membrane, scanty urine, numbness of the extremities, hyperæsthesia, paralysis, convulsions, fainting, and death.

In the *Archives of Surgery* for April 1895, p. 186, there is a note by Mr. Jonathan Hutchinson on the influence of arsenic in causing keratosis of the palms and soles in a young lady the subject of lupus, and in whom the keratosis gradually disappeared on discontinuing the medicine; and in the same journal for October 1895 is reported the case of a young man who, after taking arsenic for eight years, developed numerous small corns and a peculiar horny condition of the palms and soles, which on microscopical examination showed great thickness of the epidermis, but no disease of the papillæ. There is now a considerable amount of evidence to show that in addition to peripheral neuritis, bronzing of the skin, and the development of keratosis, the prolonged administration of arsenic may be productive of even more serious consequences. In the *Archives of Surgery*, vol. v. p. 339, allusion is made to a case of Mr. Arbuthnot Lane's; namely, a man who, after taking arsenic for thirty years in order to relieve a psoriasis, became the subject of multiple growths of epithelial cancer. Dr. Allbutt has seen a similar result in a young woman. It appears that the keratosis and multiple small growths that develop in the skin after a lengthened course of arsenic are peculiarly prone to take on malignant action. Whilst, therefore, arsenic causes marked thickening of the skin it is indirectly responsible for growths which subsequently become true epithelial cancer. It may also cause other forms of skin irritation. Wood mentions a case of obstinate eczema of the hands consequent upon using playing-cards containing on the back one-eighth grain of arsenic each.

The diagnosis of chronic arsenical poisoning is at times extremely difficult. Peripheral neuritis and progressive emaciation, without local disease, are either diathetic or toxic. A chemical examination of the urine may throw light upon a doubtful case.

Morbid Anatomy.—No matter by what channel arsenic has entered the system, the mucous membrane of stomach and intestines is the seat of very marked changes: it is swollen and congested; it may be the seat of numerous ecchymoses, small emphysematous bullæ, or diphtheritic exudation. The œsophagus generally escapes. If arsenic has been taken in the solid form, crystals are frequently found adhering to the mucous membrane. Long after death, months it may be, the inflammatory changes of the mucous membranes can be recognised owing to the antiseptic and preservative powers of the drug; but care must be taken to discriminate between this and the peculiar redness observed in healthy stomachs undergoing putrefactive changes. The whole of the intestinal tract in arsenical poisoning may be so reddened that the lesions may closely resemble those of cholera; a resemblance which even microscopical examination does not remove, for equivocal micro-organisms have been found in the epithelial flakes. Fatty degeneration of the intestinal epithelium and a swollen condition of Peyer's patches and of the solitary glands may also be present. Arsenic has thus a peculiarly selective influence upon the gastro-intestinal tract. That the lining membrane of the stomach actively excretes certain chemical bodies has been shown by Kandikoff of St. Petersburg, who demonstrated that if arsenic, for example, were injected into the rectum it was absorbed and subsequently discharged by the mucous membrane of the stomach. To kill an animal by means of arsenic, a larger quantity has to be injected into a vein than if the drug is given by the mouth. This peculiar behaviour of arsenic is probably due to the fact that when the drug has been absorbed into the blood it is separated by the gastric mucous membrane, and in its passage outwards it exercises an irritant action, setting up inflammatory redness.

A widespread fatty granular degeneration, again, is characteristic of arsenical poisoning. It affects the liver and kidney, the intestinal epithelia, and voluntary muscular fibre. The degeneration is sometimes as marked as that met with in phosphorus poisoning. Binz considers that cellular protoplasm has the power of oxidising arsenious to arsenic acid, which is again reduced to arsenious acid. In this way, owing to a series of repeated oxidations and reductions, the protoplasm undergoes a fatty change. There are no facts to support this opinion. Arsenic uniting with protoplasm may not form an albuminate, yet it enters into such close chemical union with it that the protoplasm is destroyed. Besides the widespread fatty degeneration of the liver, Salkowsky found that its glycogenic function was destroyed; but in my experiments glycogen was found in the liver after death.

Whilst arsenic is rapidly eliminated from the system, the channels of escape being the gastric mucous membrane, kidneys, skin, and saliva, sufficient is yet retained within the system to allow of its detection post-mortem; although fatal cases of arsenical poisoning have been recorded without the metal having been found. This is a point of considerable importance from a medico-legal point of view. In the case of my own dog, which took arsenic every day for months, and which before its death suffered from vomiting, diarrhœa, and rapid emaciation, the most careful chemical examination of the liver and bones conducted by

Professor Bedson and Mr. F. C. Garrett, repeated on three occasions, failed to detect the slightest trace of arsenic. This is a circumstance of more than passing interest. In cases of criminal poisoning, therefore, there is no justification for the plea set up by the defence, that unless an amount of poison were abstracted from the liver, sufficient of itself to be regarded as a fatal dose, the cause of death could not have been arsenical poisoning. Arsenic has been detected in the bile, the sweat, the tears, and in the serosity of a blister; but the urine is the medium by which it principally escapes from the body, hence the improbability of any extensive accumulation of arsenic. Given, therefore, a case of suspected poisoning by arsenic, the urine of the patient should be examined by Reinsch's test. In using this method the following points should be attended to: (*a*) reduce 12 to 16 ounces of urine by gentle evaporation to $\frac{1}{4}$ of its bulk; (*b*) add $\frac{1}{6}$ to $\frac{1}{8}$ of its bulk of hydrochloric acid known to be free from arsenic; (*c*) dip into it a bright piece of copper foil and boil for at least 15 minutes, when (*d*) if arsenic be present the copper will exhibit a grayish stain. If arsenic be present in large quantity a glistening, black-lead appearance may be obtained; but, as mercury, sulphur, selenium, and antimony produce a similar effect, the copper foil must be submitted to the test of sublimation. Should the stain be due to mercury the metal sublimes in microscopic globules; if to sulphur it will rub off upon the finger; if to arsenic it dissolves in caustic ammonia, which sulphide of copper will not do. The arsenical stain, when sublimed, gives a crystalline deposit of arsenious acid; the antimonial stain is bluer and gives no crystalline sublimate.

In poisoning by white arsenic a microscopical examination of the vomit may be of considerable assistance. Numerous small, white particles are frequently observed which, when picked out by the forceps, carefully washed, dissolved in boiling water, and allowed to cool, crystallise out as small octahedra of arsenious acid. From these when heated with soda on a piece of carbon in the reducing zone of the flame of a blow-pipe a garlic odour is evolved. For fuller details of the longer and more accurate methods of testing for arsenic in organic substances known as Reinsch's or Marsh's, the reader will consult text-books on toxicology.

Into the question of the imbibition of arsenic after death we need scarcely enter, there being few arguments and fewer facts to support the assumption. In courts of law it has been maintained that corpses may absorb arsenic from the earth—the theory being that though arsenic in the soil is in the form of an insoluble compound, it might combine with calcium to form the arsenite of lime, which, becoming soluble through the action of carbonic acid evolved from decaying vegetables, might filter down to the corpse. Sonnenschein's experiments indicate the improbability of such an occurrence.

Treatment.—If the case be acute and seen early, emetics and the use of the stomach-pump are called for; but the antidote for arsenical poisoning, when the drug is still present in the stomach, is freshly prepared ferric hydrate. It acts by converting soluble arsenious acid into the insoluble arseniate of iron. Should the poison have already passed into the system ferric hydrate is useless. The treatment must then depend upon the symptoms. Copious draughts of water probably aid the elimination of the drug by the kidneys. Ferric hydrate is rapidly prepared by adding liquor ammoniæ fortior to the liquor or tincture of the perchloride of iron, care being taken not to add excess of ammonia. The liquid may be administered without filtration and given freely. For arsenical paralysis tonics such as liquor strychniæ may be necessary; as well as the employment of massage and electricity. Iodide of potassium may be of service as an aid towards the elimination of the poison in mild subacute cases.

Thomas Oliver.

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T. O.

INTERNAL PARASITES

PSOROSPERMOSIS

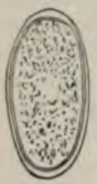
WORMS

A. PLATYHELMINTHES
B. NEMATHELMINTHES

PSOROSPERMOSIS

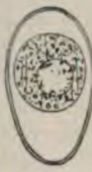
THE prevalence of a disease caused by psorosperms, or coccidia, in the lower animals, and the occasional occurrence of a similar disease in the human subject, make us regard psorospermosis as worthy of clinical recognition. It is allied to tuberculosis in being caused by the invasion of the tissues of the body by an organism from without; in being at first a local disease; and in having a tendency, slight it is true—not nearly so great as in tubercle—to invade the system and become diffused throughout the different tissues of the body, ultimately causing death. The tubercle bacillus, however, differs from the psorosperm in selecting for its habitat the vascular connective tissues of the body, namely, the cancellous parts of bones and the lungs: whereas the psorosperm invades the epithelial cells covering the mucous membranes or the skin; but, by extension into the subjacent connective tissue it may enter the lymph or blood channels, and thus be disseminated throughout the body. Although, therefore, in some respects a similarity exists between the two diseases, yet their action differs essentially in one particular at least; namely, in the kind of tissue first invaded. Nevertheless, we may regard psorospermosis—as we regard tuberculosis—as a local disease which, under suitable conditions, may become general and spread throughout the tissues of the body. As a local malady it is met with (*a*) as Darier's disease of the skin and chronic eczema of the nipple (Paget's disease) [see section on Skin Diseases]; (*b*) in the mucosa of the intestinal canal, and that of the urinary tract; and (*c*) in the liver, from which organ general infection is most likely to occur.

The pathology of this disease has been chiefly studied in the rabbit, in which animal it is very prevalent in the wild as well as the domesticated state. Hake, in 1839, gave a very clear description of this condition, illustrated by drawings of dissections and of microscopic specimens; but not until some years after were the peculiar bodies described by him identified as psorosperms. The disease chiefly affects the liver; and there it is characterised by the presence of numerous minute, firm nodules scattered more or less uniformly throughout its substance. The nodules vary in size up to one-third of an inch or more in diameter; and, although the smaller ones are firm, yet the larger ones often contain a central soft caseous or semi-puriform mass which can be expressed or scraped out. Each nodule is found to be a small bile-duct locally distended, its walls thickened, and its lumen filled with epithelial cells and psorosperms. In the larger nodules the mucous lining of the bile-ducts, in the epithelial cells of which the psorosperms grow and flourish, is thrown into papillary folds; and the connective tissue around is much increased and condensed. It is but rarely that the psorosperms, so abundant in the epithelial lining, find their way into the surrounding hepatic structure. In the soft interior of the larger nodules there are innumerable clear ovoid bodies with highly refracting, double-contour capsules, either free or contained in enlarged, cystic, and otherwise altered epithelial cells. These bodies measure on an average from 30 to 40 μ in length, by 15-20 μ in breadth; and often, at the narrower end, there is an indication of a micropyle. They may be found in one of three states, according to the degree of maturity they have attained. In the less mature form (Fig. 14, A) the contents are uniformly granular; in (Fig. 15, B) the granular contents are gathered into a rounded nucleated mass in the centre of the capsule; and in the mature form (Fig. 16, C) the granular contents are replaced by four psorosperms. The last form, in which the psorosperms lie in a quiescent state, is ready to undergo further development, and simply awaits the suitable conditions. The further changes consist in dehiscence of the capsule and escape of the psorosperms, which in their turn give rise to minute amœboid bodies, smaller in size than a white blood corpuscle. Leuckart thinks this dehiscence takes place in the stomach by virtue of the influence of the gastric juices upon the double-contour resisting capsule, the coccidia being introduced into the body with grass or green vegetables, probably contaminated with the excreta of infected rabbits. When the psorosperms have made their escape from the mature coccidia their spores enter the epithelial cells and there grow, and ultimately produce the mature coccidia form. Whether all these changes can take place in the tissues, for example in the bile-ducts of the liver, or whether it is necessary that the mature coccidia should pass through the body or tissues of another host, is not as yet satisfactorily determined. Amongst the Protozoa these parasites belong to the sub-class Coccidiidea (Butschli) of the Sporozoa; and though they resemble those of another sub-class, Gregarinidæ (Butschli), yet they are not identical with them, the latter being parasitic upon invertebrates. In the rabbit's liver, for example, the mature psorosperm is called *Coccidium oviforme* (Leuk).



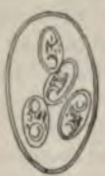
A.

Fig. 14.



B.

Fig. 15.



C.

Fig. 16.

A place is given to psorosperms in this work on account of their power to produce disease in the tissues of the human body as well as in those of the lower animals, disease which may resemble malignant disease.

In man disease produced by psorosperms has been observed in several instances; and the symptoms to which they give rise depend upon the extent of the disease and upon the tissue concerned.

As a local disease it may be met with in the *liver*, as in the rabbit; and thence, by causing great destruction of the liver substance and thereby disturbing the hepatic function, it gives rise to symptoms similar to those found to occur in the rabbit, if not identical with them, namely, to progressive wasting, nausea, and inability to take food; these signs of exhaustion are followed by death.

When, however, the disease affects the mucous membrane of the *urinary tract*, where it usually gives rise to the formation of multiple, minute, superficial cysts with clear contents, it may cause hæmaturia with increased frequency of micturition; or it may partially block the ureter and thus produce hydronephrosis with its attendant symptoms.

Again, when the *intestinal mucous membrane* is affected the epithelium is occupied, as it is in the bile-ducts, with psorosperms in various stages of development; and there may be, moreover, as in the rabbit, inflammation of the mucosa, and even superficial ulceration attended with dyspepsia, irritability of the bowels, more or less constant diarrhœa, hæmorrhage, exhaustion, and ultimately death.

As a general disease. — Psorospermosis has but few features to distinguish it during life from other and similar local diseased conditions; still less characteristic are the symptoms when the spores, making their way into the circulation, become diffused throughout the body, attacking serous membranes, brain, spleen, heart-muscle, and so on. A few such cases have been clinically recorded; and from these we may gather that the chief symptoms of general infection by psorosperms are—pains in the limbs, headache, drowsiness and possibly delirium, furred dry tongue, nausea and perhaps vomiting, albumin in the urine, increase of both liver and splenic dulness, and remittent fever, not reaching, however, to a high degree (103°). These symptoms end in death after a period varying from two to seven or more weeks. Though they are not so severe nor so acute, they resemble those produced by the general infection of tuberculosis, and also those described as the "typhoid state."

For further information as to the course taken in the cases hitherto recorded in man, and for fuller particulars concerning the disease in the lower animals, I would refer the reader to the important papers which are indicated in the subjoined list rather than attempt to distinguish more minutely the symptoms produced either by local or by general psorospermic infection.

JOSEPH GRIFFITHS.

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J. G.

WORMS

THE larger entozoa, for the most part visible to the eye, which infest mankind, with rare and unimportant exceptions, belong to the sub-kingdom vermes or worms. The distinguishing zoological features of this group of organisms are *a bilateral, unsegmented or uniformly segmented body, having a dermal muscular system and a paired excretory system (water vascular); skeleton and articulated appendages are wanting.*

The worms are divisible into several classes, but only two of these classes occur as parasites in the body of man, namely, 1st, **Platyhelminthes**, which may be defined as *worms with a flat, elongated body, very generally provided with hooks, or suckers, or both; they possess a cerebral ganglion, and, as a rule, are hermaphrodite;* 2nd, **Nemathelminthes,** *round worms with a tubular or filiform body, the cuticle of which is often ringed; the head end may be provided with hooks or papillæ; the sexes are separate.*

Of the **Platyhelminthes** two orders are found parasitic in man—1st, *Cestoda*, or tapeworms; 2nd, *Trematoda*, or flukes. Of the **Nemathelminthes** only one order is represented, namely, *Nematoda*, or threadworms.

The following list of species, arranged in accordance with this classification, embraces all the more important and well-authenticated worms which, up to the present, have been found parasitic in man.

WORMS

PLATYHELMINTHES.

Cestoda.

Family—TÆNIADA.
Tænia mediocanellata.
Tænia solium.
Tænia nana.
Tænia flavo-punctata.
Tænia madagascariensis.
Tænia cucumerina.
Tænia acanthotrias.
Tænia echinococcus.

Family—BOTHRIOCEPHALIDA.
Bothriocephalus latus.
Bothriocephalus cristatus.
Bothriocephalus cordatus.
Bothriocephalus Mansoni.

Trematoda.

Family—DISTOMIDA.
Distomum crassum.
Distomum hepaticum.
Distomum lanceolatum.
Distomum ophthalmobium.
Distomum heterophyes.
Distomum hæmatobium.
Distomum Ringeri.

Family—DISTOMIDA (*cont.*)
Distomum sinense.
Distomum conjunctum.

Family—AMPHISTOMIDA.
Amphistomum hominis.

NEMATHELMINTHES.

Nematoda.

Family—ASCARIDA.
Ascaris lumbricoides.
Ascaris mystax.
Ascaris maritima.
Oxyuris vermicularis.

Family—STRONGYLIDA.
Eustrongylus gigas.
Strongylus longevaginatus.
Ankylostoma duodenale.

Family—TRICHOTRACHELIDA.
Trichocephalus hominis.
Trichina spiralis.

Family—FILARIDA.
Filaria inermis.
Filaria oculi humani.
Filaria loa.
Filaria restiformis.

Family—FILARIDA (*cont.*)
Filaria hominis oris.
Filaria labialis.
Filaria lymphatica.
Filaria medinensis.
Filaria volvulus.
Filaria diurna.
Filaria perstans.

Family—FILARIDA (*cont.*)
Filaria nocturna (F. Bancrofti).
Filaria Demarquaii.
Filaria Magalhaesi.

Family—ANGUILLULIDA.
Rhabditis Niellyi.

Family—RHABDONEMIDA.
Rhabdonema intestinale.

It would be impossible in the limited space at my disposal to give anything like a complete account of the individual parasites composing this long list. For this the reader is referred to the standard systematic works on helminthology. The most I can hope to supply is such a description of the physical features of the more important of these organisms, of their respective life-histories, and of their associated clinical phenomena, as will enable the reader to arrive at a correct diagnosis in cases of entozoal infection; and, at the same time, enable him to advise intelligently on the important practical subjects of prophylaxis and treatment.

CLASS I.—PLATYHELMINTHES.—**Order, Cestoda.**—The cestodes or tapeworms are long, flat, white, ribbon-like organisms which, in their mature form, inhabit the alimentary canal of most vertebrates.

Each worm, anatomically speaking, is divisible into a head and neck —*scolex*, and, springing from this, a single file of joints or segments—*proglottides;* together these constitute the body or *strobila*. The head is provided with two or four strong muscular discs or *suckers*, and, in most species, arranged around a beak or *rostellum*, one or more circles of chitinous *hooklets*. These, the suckers and hooklets, serve to attach the parasite to the mucous membrane of the alimentary canal of the host.

The head is very minute, being, as a rule, just discernible with the naked eye as a sort of intumescence or bud at the free end of the narrowest or uppermost part of the worm. Tracing backwards from the head or scolex, and originating from its posterior part by a sort of process of serial budding, we first come to minute immature proglottides. The farther we proceed backwards the proglottides become more distinctly differentiated, increase in size, and show more and more evidences of progress towards maturity. Finally, and long before we arrive at the last elements of the chain, we find that the proglottides are sexually mature, each proglottis possessing elaborate male and female organs of reproduction, the latter being laden with eggs. A tapeworm may therefore be regarded as a colony, and each individual proglottis as an animal complete in itself.

The proglottides contain no organs of digestion, nutrition being effected by absorption from the alimentary juices of the host. Excretion is carried on by an elaborate water vascular system.

The male organs of generation consist of testis, vas deferens, and cirrhus (penis); the female of ovary, yolk gland, shell gland, uterus, receptaculum seminis, and vagina. The vagina and vas deferens usually open into a common cloaca, which, in its turn, opens externally either on the ventral surface, or alternately on the right or left margin of the proglottides. In some species the male and female genital pores are separated.

When the ova have arrived at maturity the proglottides containing them break off in ones or twos, or in strings, and pass out of the body of the host either by their own proper movements or, more usually, are expelled with the fæces. They are easily recognised as white, oblong, or square bodies which indulge in movements more or less active. The ova they contain are either expelled by the contractions of the proglottides attending these movements, or they may not be set free until the proglottides are swallowed and digested by some animal, or have decomposed.

As a rule, in most species at this stage, the only element remaining of the original egg is the embryo—now enclosed in a thick shell of its own, the yolk and yolk membranes having disappeared at an earlier stage of intra-uterine life. In a few species the ovum at the time of its birth is still entire, and the embryo still undeveloped. In the former the differentiated embryos are ready to enter the body of their intermediate host; in the latter, before they reach this stage, the ova have to pass a certain time in water or in some other medium during which the embryo is elaborated in preparation for this migration.

The embryo of the cestodes is provided with six hooklets (hence the term "hexacanth") arranged in pairs at one pole of its spherical body. On arrival in the alimentary canal of its intermediate host, the shell in which the embryo is enclosed is dissolved, or in other cases the mantle of cilia with which it is invested is cast. By means of the hooklets it then works and bores its way through the walls of the gut and the intervening tissues until it arrives at the liver, lungs, muscles, brain, connective, or other appropriate tissue. The six hooklets are now discarded, and from the pole opposite to that occupied by these hooklets, and by a process differing in detail according to species, a head and neck (scolex), exactly similar to that of the tapeworm from which the embryo originally emanated, is developed.

When this stage is completed it is found that the scolex springs from a large, clear, watery bladder,—really the dropsical body of the embryo,—into which it can be drawn, and from which it can be protruded. This is called a *cysticercus*, and tapeworms so characterised are classified as *cystici*. In another set of tapeworms this cyst is exceedingly minute and rudimentary; such are classified as *cystoidei*. In a third set the embryo becomes enormously distended by a clear watery fluid; by a sort of budding process from the inner cellular layer of the wall of the cyst containing this fluid a number of subsidiary *brood capsules* are formed, the inner layer of which gives origin to tapeworm scolices. These cysts are designated *echinococcus*, and the genus *echinococcifer*. Yet a fourth type of development is supplied by the *bothriocephalidæ*. In them no cyst of any description is formed; the embryo simply enlarges and elongates, the head with two suctorial grooves being formed at one end. In these worms the immature parasite may attain considerable length in the intermediate host—several inches perhaps, and resemble in some respects the mature tapeworm.

Many cestodes at this stage of development retain for years their capacity for further advance when transferred to the stomach of the definitive host; others again die at a comparatively early date, becoming withered and calcified. On transference to the definitive host the cystic structure is digested off, and the scolex, by means of hooks and suckers, anchors itself to the mucous membrane of the small intestine and rapidly grows into a mature tapeworm.

The **cestoda** are represented in man by two families, the *tæniadæ* and the *bothriocephalidæ*. The former have four suckers, and usually a single or double row of hooklets on a rostellum. In them the sexual opening is marginal. In the young stage they possess a caudal cyst. The *bothriocephalidæ* have only two suckers, and, as a rule, their sexual organs open on the surface of the proglottides. As already explained, in their immature stage they possess no caudal cyst, but lie free or lightly encysted in the tissues of the intermediate host.

Practically we have to deal with only three species of tapeworm: **Tænia mediocanellata,** or the beef tapeworm; **Tænia solium,** or the pork tapeworm; and **Bothriocephalus latus**, or the fish tapeworm. Besides these a number of other cestodes have been met with in man; and, doubtless, as our acquaintance with the helminthology of savage and semi-civilised peoples extend, yet others will be added to the list. Though of interest scientifically, these rarer tapeworms appear as yet to have little practical importance.

Tæniadæ—(*Cystici*)

Tænia mediocanellata (Fig. 17)—(Synonyms: *T. saginata*, *T. inermis*, *Tæniarhynchus mediocanellatus*).—This is one of the commonest and most widely distributed of the human tapeworms. According as it is elongated or contracted, it measures from 4 to 8 metres in length, and is composed of from 1200 to 1300 proglottides. The more mature proglottides are long (18–14 mm.) and thick; those about the middle of the worm are broad (12–14 mm.); those constituting the more immature portion gradually taper in size to very narrow and extremely delicate dimensions. The pear-shaped head (Fig. 18, A and B) (1·5–2 mm.) is provided with four powerful suckers, but has neither hooklets nor rostellum. The marginal genital pore projects markedly, and leads to a uterus having many—twenty to thirty—lateral dichotomously dividing branches. The contained eggs, or rather shelled embryos, are minute (0·03 mm.), slightly oval bodies. The shell is thick and made up of innumerable little rods; it encloses a six-hooked embryo.

Carefully-conducted feeding experiments have conclusively proved that the ox acts the part of intermediate host to *T. mediocanellata*, the cystic stage of the parasite being accomplished in the muscles of this animal; more rarely in the liver and other viscera. It is not known how long the cysticerci retain their vitality, several years probably, before becoming shrivelled and undergoing calcareous changes; but it is known that when man consumes raw or imperfectly cooked beef containing living cysticerci, and before this degeneration has occurred, *T. mediocanellata* is developed in his intestine.

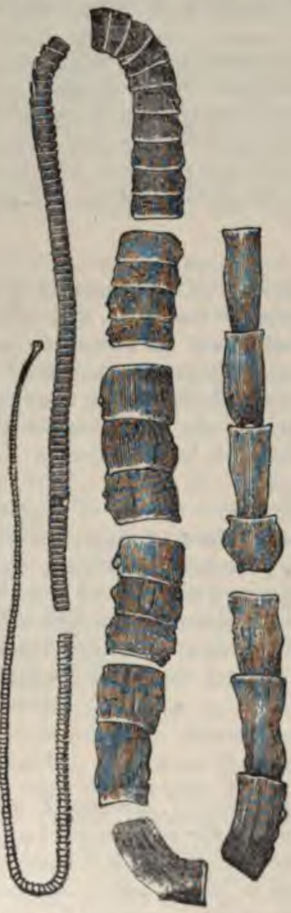


FIG 17.—*T. mediocanellata* (nat. size). After Leuckart.

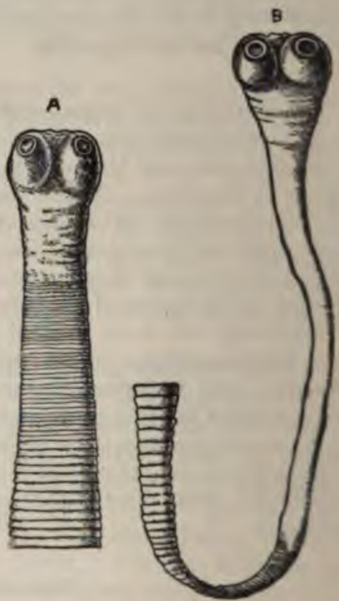


FIG. 18.—Head of *T. mediocanellata*. A, contracted; B, extended (×8). After Leuckart.

Thus it comes about that in countries in which much and imperfectly cooked beef is eaten this tapeworm is very prevalent; more particularly is this the case where the cattle are badly fed and tended, and where they are therefore in their turn much exposed to infection by tapeworm ova. Comparatively rare in Western Europe and the United States of America, *T. mediocanellata* is common in Eastern Europe, in Asia, Africa, and parts of South America. In many districts it is excessively common. In Abyssinia, for example, nearly every native entertains one or more of these unpleasant guests. In the North-West Provinces of India, where about 5 per cent of the cattle are affected with cysticerci, it is nearly as prevalent,—a condition entirely attributable to the filthy habits of the people, their carelessness in the management of their cattle and in the cooking of their food, and their personal uncleanliness. Of late years this tapeworm is said to be becoming more common in the south of France in consequence of the large importation of Algerian bullocks.

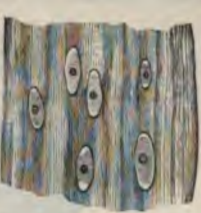


FIG. 19.—Cysticercus of *T. mediocanellata* in beef (nat. size). After Leuckart.

Measly beef (Fig. 19), that is beef affected with *Cysticercus tænia mediocanellata*, is easily recognised. Here and there, scattered throughout the muscles and lying lengthwise between the fibres, small, oblong, watery cysts, scarcely measuring 1 cm. in length, are to be seen. If one of these cysts is shelled out and examined with a lens, the invaginated head of the immature cestode can be detected in its inside. By placing the cyst in warm water the head becomes evaginated (Fig. 20), and is seen to be attached to the end of a long neck springing from the short equator of the cyst. Under the microscope the four suckers and unarmed head of *Tænia mediocanellata* are readily recognised.

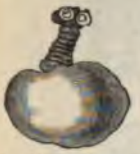


FIG. 20.—*Cysticercus T. mediocanellata*; head evaginated (×3). After Leuckart.

Cysticercus T. mediocanellata, unlike the cysticercus of *T. solium*, is not known to occur in man. The only animals besides the ox in which it has hitherto been found are the goat and the giraffe. Attempts to rear the tapeworm in the dog have failed.

It has been proved that from the time the cysticercus is swallowed to the appearance of proglottides in the stools about sixty days must elapse. At the end of this time eight or twelve or more proglottides are thrown off daily by the now mature worm during an indefinite number of years. The proglottides rarely appear in the stools in strings, as with many other tapeworms; they are usually given off singly, sometimes passing out of the bowel independently of the act of defecation and by their own proper locomotive activity. Thus, besides being nearly a constant feature in the stools, they may creep about the body, and are frequently found in the patient's clothes, in his bed, or about his room. During their wanderings the remarkable elongations and shortenings and muscular contractions of the proglottides bring about the expulsion of the eggs—very commonly from a rupture in the fore part of the uterus. In this way these eggs are strewn about, and, if fortune favour them, are placed for ingestion by the ox.

A knowledge of the facts of the life-history of this, as of all other parasites, is of extreme importance, as indicating with precision the direction that prophylactic measures should take.

Tænia solium.—This tapeworm is distinguishable from the foregoing by its smaller size (3–3·5 metres), but especially by the double circle of twenty-six to twenty-eight hooklets which surrounds the medium-sized rostellum (Fig. 21). The spherical head (1·0 mm.) carries four large somewhat prominent suckers. The neck is thread-like, the segments very gradually increasing in size up to about the middle of the worm where they measure rather under 8 mm. in breadth. Towards the free end the ripe proglottides (Fig. 22) elongate and become narrower, measuring there from 10 to 12 mm. in length by 5 mm. in breadth. The genital pore is marginal. The uterus has on each side seven to ten lateral branches which divide dendritically. The eggs, or rather embryos, are spherical (0·03 mm.), and have a firm, thick, brownish shell, covered with countless little rods.

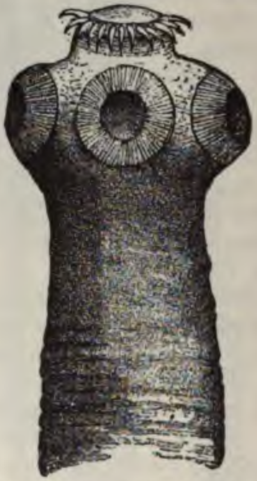


FIG. 21.—Head of *T. solium* (× 45) After Leuckart.

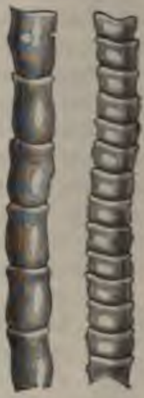


FIG. 22.—Ripe and half-ripe proglottides of *T. solium* (nat. size). After Leuckart.

The proglottides as they fall ripe are discharged singly or in chains with the fæces of the host, and in this way the ova, while still in the proglottides, or, after expulsion from them during their slow movements, get an opportunity of being transferred to the stomach of the pig or, occasionally, of other animals, including man himself.

Arrived in the stomach of a vertebrate the shell enclosing the six-hooked embryo is dissolved by the gastric juices. Being thus liberated the embryo works its way through the gut and into the viscera, muscles, and connective tissue of the intermediate host. The connective tissue between the muscular fibres seems to be the more normal and usual destination for the embryo, but it may come to rest in almost any organ. When it comes to rest in a muscle the embryo becomes transformed in the course of a few weeks into a clear, elliptical cyst (8–10 mm.) separating muscular bundles, and disposed in same direction (Fig. 23). This cyst contains the spirally rolled and much-wrinkled invaginated cestode head, which, in hooks, suckers, rostellum, and in every other respect, resembles the scolex of *Tænia solium* (Fig. 24).

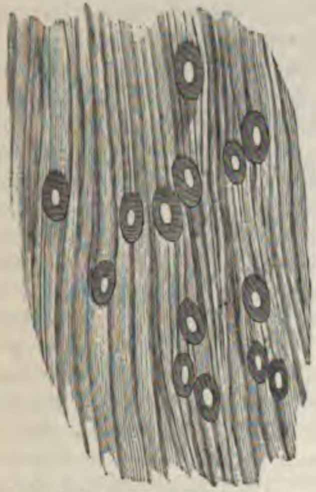


FIG. 23.—Cysticercus of *T. solium* in pork (nat. size). After Leuckart.

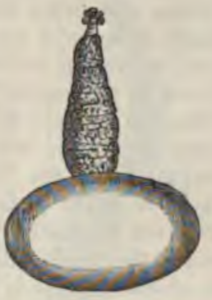


FIG. 24.—*Cysticercus T. solium*; head evaginated (×2). After Leuckart.

Pork beset with these cysticerci—the long and well known *Cysticercus cellulosæ*—is known as "measly pork." When eaten raw, or imperfectly cooked, it leads in man to the development of *Tænia solium* in the intestine, as has been amply proved by feeding experiments. It is a comparatively rare thing, in Europe at all events, to find more than one *Tænia mediocanellata* in the same individual host; hence this tapeworm is sometimes called the *ver solitaire*. It is otherwise with *Tænia solium*—two, or many more, being frequently found together.

The geographical distribution of *Tænia solium* corresponds with that of the pig; its greater or less abundance in any particular district or country depending on the way the swine are tended, the habits of the natives as regards the disposal of their dejecta, and the way in which they prepare their pork for the table. In 3814 post-mortem examinations in North Germany the mature tapeworm was found about once in every 200 bodies. In South Germany, in France, in Great Britain, and in the United States, it is by no means so frequent. Naturally the *Cysticercus cellulosæ* has a corresponding geographical distribution. According to Leuckart, in Prussia, in 1,728,600 swine examined in 1876 one carcase in every 370 had *Cysticerci cellulosæ*. As regards man, in 9753 post-mortem examinations of human bodies in various Pathological Institutes in North Germany, the cysticercus was found once in every 76 bodies. In Western Europe their occurrence is not nearly so common. The greater frequency of cysticerci in man, as compared with the pig, is of course attributable to the greater care with which they are searched for in the former, and to his greater age; not to his superior susceptibility or greater liability.

In consequence of the liability of man to cysticercus infection through his swallowing the eggs of *Tænia solium* in food or in water, or from their introduction by soiled hands, or, as some suggest, by a sort of auto-infection from the regurgitation into the stomach of the ripe proglottides of the tapeworm during an act of vomiting, or in other ways; and in consequence of the frequency with which the *Cysticercus cellulosæ* develops in the brain, eye, heart, and other localities (rarely in the liver, never in the bones), it becomes an object of considerable pathological importance. Cases are on record in which hundreds and even thousands of cysticerci were found in the various organs. Such wholesale infection is, however, rare. Strange to say, the parasite seems to have a predilection for the brain and eye, and in not a few instances it has been found restricted to these organs. In the brain the cysticerci are usually found in the membranes or in the cortex, more rarely in the interior. In eighty-eight cases collected by Küchenmeister they were found forty-nine times in the membranes, thirty-nine times in the cortex, thirty-six times in the great ganglia, nineteen times in the central substance, and eighteen times in the ventricles. Von Graefe calculated that in Berlin ophthalmic practice the cysticercus was observed in the eye once in about every thousand cases. In England they are very much rarer. Their most common position in the eye is beneath the retina; about half as frequently they are found in the vitreous humour; still more rarely they appear in the anterior chamber and elsewhere. In the aqueous and vitreous humours the parasite is free, and the movements of the head and neck can readily be made out. In these cases it is probable that in the first instance the cysticerci were developed behind the retina, or in the iris, and that afterwards they had broken loose.

Cysticerci developed in the arachnoid or pia mater assume sometimes a peculiar branched appearance which has gained for them the name of *Cysticercus racemosus*, a name very apt to be misunderstood. In this situation the immature parasite may grow to a great size (8–25 cm.) and have many branches and diverticula. The peculiar form of this variety of cysticercus is probably attributable to the conditions of the pressure under which it grows; conditions which appear to regulate the size and shape of these cysts in the different localities of the body wheresoever they chance to be located. In the ventricles of the brain it may grow to be as big as a pigeon's egg.

Occasionally the cysticerci develop under the cutis, where they form small tumours the size of a pea. The concurrence of such tumours, or of a cysticercus in the eye with cerebral symptoms is a valuable point in determining the diagnosis of obscure brain disease.

Unless removed early, cysticerci in the eye ultimately lead to destruction of the organ, and perhaps to sympathetic inflammation of the other eye. In the heart they may give rise to functional irregularities, and even to valvular insufficiency. In the lungs they may produce asthmatic affections. In the brain, particularly where located in the central ganglia, or where they press upon nerve-trunks, or motor or sensory tracts and centres, they may give rise to paralytic or epileptic conditions; when on the surface of the brain they are usually of less moment.

Tænia acanthotrias. — This worm is known in the cysticercus stage only, and has once only been met with; namely, in the muscles, under the skin, and in the brain of a white woman from Virginia, U.S.A. In appearance it resembled the cysticercus of *Tænia solium*; but as the scolex carried from forty-two to forty-eight hooklets, arranged in a triple circle around the rostellum, it is manifest that it belonged to quite another species of cestode.

Tænia echinococcus (*Echinococciferi*).—See art. on Hydatids.

Tænia nana (*Cystoidei*).—Grassi has lately shown that this tapeworm is identical with *Tænia murina* of the rat. As a human parasite it was first discovered by Bilharz, in 1851, in the ileum of an Egyptian boy. It is the smallest of all the tapeworms infesting man, measuring only from 12 to 20 mm. in length by 0·5 mm. in breadth. The spherical head (0·3 mm.) carries four suckers and a very prominent rostellum, often invaginated, surrounded by a single circle of from 22 to 28 minute hooklets. The joints, which are short and broad, number from 150 to 170; they have a marginal genital pore, and where approaching maturity possess thirty or more ova (0·04 mm.), containing a granular material and a six-hooked embryo (0·023 mm.) enclosed in two thin, clear, and widely-separated, firm egg-shells.

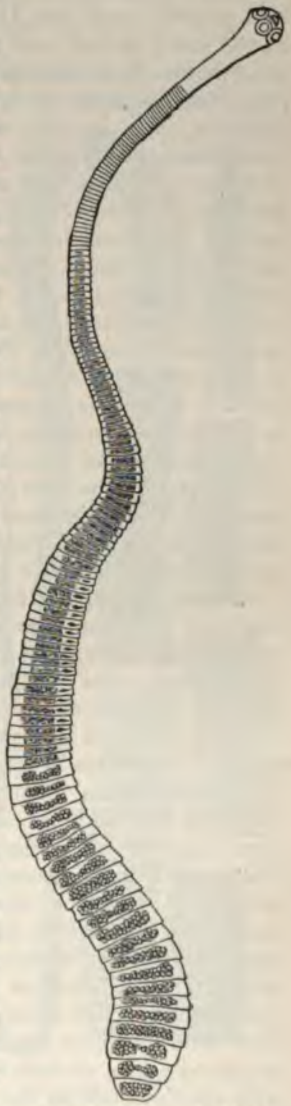


FIG. 25.—*Tænia nana* (× 18). After Leuckart.

So minute a worm has doubtless been many times overlooked; in the few instances in which its presence was ascertained it was found in hundreds. Lately cases have been reported from Belgrade, from Italy, and possibly from the United States. Grassi says it is very common in the south of Italy and in Sicily, particularly in children.

Tænia flavo-punctata—(Synonym: *Tænia leptocephala* (?)).—The occurrence in man of this tapeworm has been recorded three times in America, once in Italy, and each time in a child. Only once was the head found. This is like that of *Tænia saginata*, though somewhat smaller (0·5 mm.); it has four elliptical suckers, and is devoid of hooklets and rostellum. The neck is filiform, gradually expanding till at the posterior part of the worm the ripe proglottides—which are trapezoid, sometimes triangular in shape—measure 3 mm. in length by 4 mm. in breadth, or less. The joints in the fore part of the worm are marked by a large yellow spot—hence the name of the species. This spot is the distended receptaculum seminis. Posteriorly this mark disappears, giving place to a brownish gray colour derived from the crowd of ova which fills the joints. A notable proportion of the joints are barren. The eggs (0·06 mm.) possess a smooth, double outline, and enclose a six-hooked embryo surrounded by an oval, striated and somewhat thickish shell (0·03 mm.) The genital organs open laterally. Nothing is known of the intermediate host, which is conjectured to be some species of insect. This tapeworm, like the preceding, Grassi regards as normally parasitic in the rat, being no other than the *Tænia leptocephala* of this rodent.

Tænia madagascariensis.—Our knowledge of this tænia is still imperfect. It has been found in Mayotte (Madagascar), in Mauritius, in Siam (Bangkok), and in British Guiana. It may attain a length of 24 cm., and at the terminal proglottides a breadth of 2·6 mm. The head has four suckers and a rostellum armed with about ninety hooklets. In the interior of the proglottides the eggs are arranged in balls disposed in transverse rows. The genital pores are lateral.

Tænia canina (cucumerina).—This is more especially a parasite of the dog and cat; but it occurs in man also, and not infrequently; particularly in Scandinavia. Usually it is found in young children. The mature worm measures from 12 to 35 mm. in length. It has a long, very extensile, thread-like neck which gradually expands into segments, 1·5 mm. to 2 mm. in breadth, of a peculiar reddish tint derived from the ova they contain. The head (0·3 mm.) has four suckers and a stout, rounded rostellum carrying from forty to sixty hooklets set on disc-like bases, and arranged in three or four somewhat irregular rows. The terminal joints are much rounded at the corners, and also much elongated—four or five times longer than broad. The sexual organs, with the exception of the uterus, which is single and central, are double, with openings on both margins of the proglottis. In the dog many individuals are found together—sometimes hundreds.

Leuckart believes that the dog-louse (*Trichodectes canis*) acts as the intermediate host of this tapeworm, and that when charged with the cysticercoid parasite it is the medium for infection of the human subject. This view is probably correct, but fuller evidence is desirable.

Family—Bothriocephalida

Bothriocephalus latus (Fig. 26).—This tapeworm is of considerable size, measuring from 6 to 10, exceptionally from 12 to 16 metres in length. It is readily distinguishable from the other tapeworms infesting man by this feature, by its great breadth, by the relative shortness of the proglottides, and by the central position of the sexual openings. The head (Fig. 27) (2–5 mm. by 1 mm.) is somewhat flattened, of an elongated olive shape, and is provided with two laterally placed suctorial grooves; it has neither rostellum nor hooklets. The neck and fore part are very extensile, being thin or thicker according to the state of contraction. Traced backwards the segments gradually become broader, till about the middle of the worm where they measure 10 to 12 mm. in breadth by 4 or 5 mm. in length. Farther back the segments become narrower and elongate, so that about the free end they are nearly square. The margins of the segments are thin and flat, but the central portion is thicker, bulged out by the gravid uterus. The segments are very numerous—3000 to 4000 sometimes. In those which are riper the uterus, distended with ova, is thrown into radially-arranged folds, forming what is known as the "uterine rosette," under the middle of the fore part of which the sexual openings are to be found. These openings are two in number, and are placed close together,—the anterior, a transverse slit in which are cirrhus, sheath, and vulva, and the posterior, the punctiform opening of the uterus. The eggs are oval (0·05 by 0·035 mm.); the shell is simple, brown, and closed in at one end by an operculum.

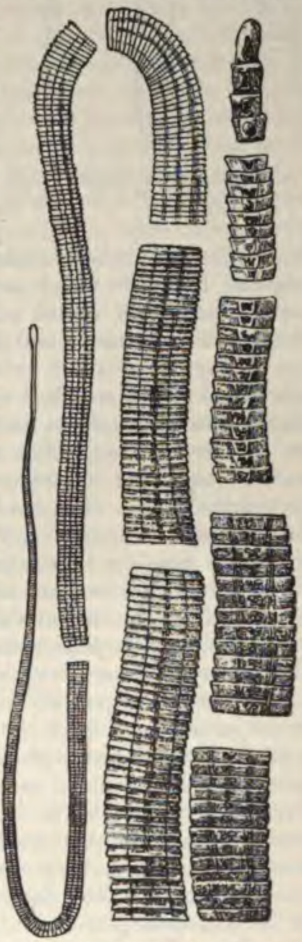


Fig. 26.—*Bothriocephalus latus* (nat. size). Leuckart.

In the other human tapeworms already described the embryo is formed in utero, and very generally the vitelline portion of the ovum has disappeared before the proglottides are detached; the embryo, in fact, enclosed in its own proper shell, is the only part of the ovum remaining. It is otherwise in *Bothriocephalus latus*. While

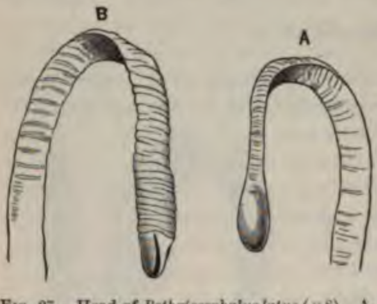


Fig. 27.—Head of *Bothriocephalus latus* (×8). A, from the flat side; B, from the margin. Leuckart.

in utero, and perhaps for months afterwards, the embryo is still undeveloped, and the egg retains all the characters proper to an ovum. To secure maturation of the ovum it has to lie in water for a longer or shorter time, according to temperature and other circumstances. A ciliated six-hooked embryo is then developed which, when sufficiently mature, effects its escape from the ovum by forcing back the operculum; it then swims about in the water like an infusorian. While in this ciliated swimming form it gains access, either directly, or possibly through the body of another animal as yet unrecognised, to certain fishes, particularly pike, burbot (*Lota vulgaris*), and probably other fresh-water species, which act as intermediate hosts to the young parasite. In these fishes young bothriocephali are often found in large numbers lying free or only feebly encysted in the viscera and muscles (Fig. 28). They have no caudal cyst, nor do they exhibit any indication of having gone through such a metamorphosis as takes place in the higher cestodes; the embryo seems simply to lose its mantle of cilia, to drop its six hooklets, and then to elongate itself, the future suckers becoming visible as depressions or slits at one end of the larva. The head and tail are usually found invaginated. The young worm grows to 1 or 2·5 cm. in length by 2 or 3 mm. in breadth. In this condition it is transferred in raw, smoked, or imperfectly cured or cooked fish to the intestine of man, dog, cat, or other ichthyophagous animal, where it rapidly develops into the mature *Bothriocephalus latus*.

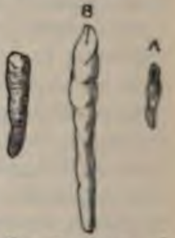


Fig. 28.—Larvæ of *Bothriocephalus latus* from the pike. A and B with extended, C with retracted head. (A, nat. size; B and C, ×2). Leuckart.

In these facts, which have been proved many times by experiment, we have the explanation of the peculiar and narrowly limited geographical distribution of this parasite, which, so far as we know, is confined to the shores of the Franco-Swiss lakes, to Northern Italy, to Bavaria, the eastern and western shores of the Baltic, Poland, Turkestan, and Japan. A few cases are reported from Ireland and the United States. In some of these countries a very large proportion of the inhabitants are affected; in St. Petersburg, it is said, 15 per cent. As the individual parasites may live a very long time, up to twenty-one years even, and as the fish containing the larval bothriocephali are frequently exported and consumed in countries outside the strictly endemic areas, *Bothriocephalus latus* is sometimes met with at a distance from its usual and endemic haunts.

Bothriocephalus cristatus.—A doubtful species described some years ago by Davaine. He met with two cases only, both of which occurred in France. It would appear that this species or variety has not been encountered since with certainty by helminthologists. The head (3 mm. × 1 mm. × 0·6 mm.) is peculiar; it is lancet-shaped and compressed laterally, both flat surfaces carrying a prominent papillated ridge or crest. This ridge divides posteriorly, forming a sort of calamus scriptorius. A well-marked longitudinal groove, formed principally by the genital pores, runs the whole length of both surfaces of the parasite, and into the angle formed by the bifurcation referred to. There are no very manifest suckers. The ova resemble those of *B. latus*. The total length is said to be under 3 metres and the maximum breadth about 9 mm.

Bothriocephalus cordatus.—Hitherto this worm has been found in man only once. This was in Greenland, where it appears to be common enough in dogs, and where, doubtless, its occurrence is dependent on the ichthyophagous habits of men and beasts. It measures about 115 cm. in length, the terminal joints being about 5 mm. square. The head (2 mm.) is described as being short, broad, and cordiform, with lateral wings having at their borders a longitudinally-placed groove or sucker. The segments attain their maximum breadth, and also reach sexual maturity, at a very short distance (3 cm.) behind the head. From the shortness of the neck the anterior end of the worm is lancet-shaped. The genital organs open ventrally.

Bothriocephalus Mansoni—(Synonyms: *B. liguloides*, *Ligula Mansoni*).—This is the larval form of an unknown species of bothriocephalus. In making a post-mortem examination of a Chinese, in Amoy, I found a number of specimens of this parasite under the peritoneum in the neighbourhood of the kidneys and iliac fossæ, and also one apparently free specimen in the pleural cavity. They were more or less coiled up and irregularly disposed in the subperitoneal fascia, and looked like ribbon strings of pale fat underneath the serous membrane. On being turned out they were found to be long, white, ribbon-shaped parasites, with feeble yet distinct movements. No differentiated head, no definite structure, and no evidence of sexual organs were discovered, neither was there any attempt at segmentation. When fresh the parasites measured about 30 to 35 cm. in length, by about 2·5 mm. in breadth. They tapered slightly towards one end; at the broad end there was a sort of papilla which in some instances was retracted. Scheube extracted a similar parasite from the urethra of a Japanese.

Leuckart suggests that the host of the mature form of this parasite is a carnivorous animal closely associated with man. Sonsino found a similar, if not the same parasite in an Egyptian jackal.

Symptoms produced by tapeworms.—In many instances of tapeworm infection the parasite appears to give rise to no inconvenience whatever, its presence being entirely overlooked, or only made known by the appearance of proglottides—singly or in chains—in the stools. Usually, however, there is complaint of colicky pains in the abdomen, perhaps of alternating diarrhœa and constipation. Nausea and other dyspeptic sensations are often complained of, particularly when the patient is fasting. In a certain proportion of cases the general nutrition suffers, or a state of anæmia may appear and be regarded as pernicious.

In not a few cases grave nervous disturbances—such as giddiness, epileptiform seizures, chorea, hallucinations, and other neuroses have been attributed to these parasites, and apparently with justice; at all events it is stated that such symptoms disappeared on the expulsion of the presumed cause. As can readily be understood, the hypochondriacal temperament is apt to dwell on such a subject, to exaggerate actual symptoms, to imagine others, and to persist in the belief that a worm is present either where no worm had ever existed, or after its complete expulsion—a sort of tæniaphobia.

It is said that *Bothriocephalus latus*—on account, probably, of its greater size—is apt to be accompanied by more marked symptoms (more especially profound anæmia — "bothriocephalus anæmia") than either *T. saginata* or *T. solium*. *T. nana* and *T. madagascariensis*—particularly the latter—are credited with causing nervous symptoms of unusual severity; the fact that they occur principally in children probably accounts for this.

For the diagnosis of species from the proglottides passed by the patient the reader is referred to the descriptions already given of the various tapeworms.

Treatment.—The number of drugs which have been employed as tænifuges is very great. Most of these are now discarded. The male fern, pomegranate root bark and its alkaloid pelletierine, kousso or cusso, pumpkin seeds, and turpentine are, in about the order stated, those most generally employed at the present day. The exact value of thymol as a tæniafuge has yet to be determined; but as this drug frequently procures the expulsion of tapeworms, ascarides, and distomes when given in ankylostomiasis, it promises to be a valuable addition to the Pharmacopœia as an efficient all-round anthelmintic.

Before administering any of these anthelmintics it is always desirable to secure an empty condition of the bowel; and it is always well to follow up their administration by a smart cathartic—preferably by salines, which clear away any mucus which may protect the worm. They do not as a rule kill the parasite, but only paralyse it, from which state of paralysis, if not quickly swept out of the intestine, it would probably recover in a short time and renew its hold, temporarily relaxed, on the mucous membrane. As most of these drugs exercise to a certain extent a toxic effect on the host, as well as on the parasite, it is always well for the patient to lie down for an hour or two, or until these toxic effects have passed away. Good rules are:—a cupful of milk instead of the usual full evening meal; early next morning the tæniafuge on an empty stomach; shortly afterwards a brisk cathartic, the recumbent position being maintained until the latter has acted; in the event of part of a tapeworm protruding at the anus it must not be pulled, lest it snap across, and the head, remaining behind, recover its hold. Dr. Ogilvie (*Lancet*, 4th August 1894) recommends a more prolonged preliminary treatment including dieting; and, with the view of removing any mucus which might protect the parasite from the action of the drug, Carlsbad salts or other saline aperient for several mornings before active treatment is begun.

Filix mas, when fresh and well prepared, is perhaps the most reliable tæniafuge we possess. The *Extractum filicis liquidum* is best given, in emulsion or in milk, in three or four doses, of half a drachm each, at intervals of half an hour; as the cathartic, calomel (five grains) with scammony (eight grains) is efficient, or a full dose of castor oil may be given with the last dose of the extract.

Pomegranate root is a good anthelmintic. It may be used either as the official decoction, or as a decoction prepared by macerating two ounces of the bruised bark in twenty-four ounces of water for twenty-four hours, and then boiling down to eighteen ounces and straining. Of the last-mentioned preparation a third part should be given at intervals of half an hour, the last dose being followed by a purgative.

A better preparation of pomegranate, and one which is coming much into use on the Continent, is the sulphate of pelletierine, prepared from the active principle of the bark. It is usually given in one dose of five to seven grains, with an equal quantity of tannic acid, in sweetened water. This is the dose for adults. For young people the dose must be considerably smaller; it ought not to be given at all to children under eight or ten. The tannin—contrary to the general impression—does not add to the anthelmintic powers of the alkaloid; it is given as a stomachic, and tends to diminish nausea and the risk of vomiting. After from a quarter to half an hour the cathartic should be administered. In from fifty to eighty per cent of cases the entire tapeworm is expelled. In toxic doses the action of pelletierine resembles that of curare, paralysing the motor nerve terminals, but not affecting muscular irritability. If the dose be too large it may give rise to vertigo, nausea, vomiting, diplopia and other visual troubles, pallor, cramps, and so forth. With the doses mentioned, and if the recumbent position be maintained for some hours, such effects need not be apprehended.

Kousso, in doses of four to eight ounces of the official infusion, is very effective when the drug can be obtained quite sound and fresh.

Oil of turpentine, in doses of from two to four drachms in emulsion, is sometimes prescribed; but it is more nauseating and otherwise more objectionable than the drugs already mentioned.

For young children a safe tænifuge is bruised pumpkin seeds: an ounce of the bruised seeds made into an electuary is not a disagreeable mixture and is readily swallowed.

After the action of an anthelmintic the head of the tapeworm should be diligently sought in the stools; for, unless this is found, there can be no assurance that the cure will prove permanent.

Order—Trematoda

The trematodes are usually flat, leaf-shaped, unsegmented platyhelminthes, possessing a mouth and a pharynx. The latter bifurcates into two simple or branched intestinal tubes which terminate cæcally. They are provided with ventrally placed suckers, and are generally hermaphrodite. In a few species the sexes are separate.

The order is divided into several families. The nature and classification of the minute parasite (0·21 mm.) found by von Nordmann in the cataract of an old woman, and named *Monostoma lentis*, is doubtful. With this possible exception, the only trematodes represented in man belong to the family *Distomidæ*. In these there are two suckers. One sucker—into which the mouth opens—is placed at the extreme fore part of the animal. In the genus *Amphistoma* the other sucker is at the extreme end of the opposite pole of the body. In the genus *Distoma* the posterior or ventral sucker is placed more anteriorly. In the subgenus *Bilharzia* the sexes are separate.

Family—Distomida

In the distomes, as stated, the mouth opens in the centre of the anterior or oral sucker. It leads to a muscular pharynx which, after a short course, bifurcates. The two simple or branched intestinal canals thus formed run backwards, one on each side of the body, to terminate cæcally some distance from the posterior end of the worm. Excretion is effected by a series of ramifying vessels which unite to form trunks terminating in a contractile vesicle, and finally opening at the posterior pole. The male organs of generation consist of testes (two), and vas deferens—the protrusible end of which forms the cirrhus or penis. The female organs of generation comprise an ovary, yolk glands (two), shell gland, convoluted uterus, and vagina. The sexual openings are placed close together in the fore part of the ventral surface close to the ventral sucker.

So far as known, all the distomes occurring in man are oviparous. The ovum at birth in some species contains a ciliated embryo; in other species this embryo is not developed until later. In either case, after leaving the uterus of the parent the ovum is carried in the discharges of the host into water or into damp soil. Here, after a variable time, the ciliated embryo is hatched out, and for a short period swims about in search of its special intermediate host. Should it succeed in finding this—usually a mollusc or crustacean—the embryo, selecting some weak point unprotected by shell or dense integument, drills its way, by means of the little beak with which it is provided, into the body of this animal, and therein, losing its ciliated covering, enlarges and becomes transformed into a *sporocyst* (a sort of hollow sac having no alimentary canal), or into a *redia*—a similar kind of structure, but provided with an alimentary canal. In the interior of sporocyst or redia, and originating from certain germ cells, tailed *cercariæ* are developed; or, it may be, another generation of sporocysts or rediæ is produced. The minute cercariæ, originating in the sporocysts and rediæ, resemble distomes in the possession of suckers and alimentary canal, but differ from the mature worm, inasmuch as they are destitute of organs of generation; and, further, in that they are provided with actively moving and powerful tails. When sufficiently mature the cercariæ spontaneously quit the sporocyst or redia. Leaving now the body of the intermediary host, they swim about in the water, or creep about in damp places until they come across a second intermediate host—mollusc, worm, insect, larva, or fish—into the tissues of which they enter, and in which, having dropped their tails, they become encysted. In some instances this second intermediate host is dispensed with, the cercariæ becoming encysted on grass or water plants; or, perhaps, they enter the body of the definitive host without preliminary encystment. However this may be, either in the body of intermediate host, or encysted on some vegetable, or in water, the cercaria finally enters the body of the definitive host. It then finds its way to its proper habitat the intestine, bile-ducts, lungs, blood-vessels, or other tissue, and rapidly develops into the sexually mature distome.

Distomum hepaticum (Fig. 29).—The normal habitat of the liver-fluke is the bile-ducts of the sheep. Occasionally it is found in a similar situation in man, more often in certain ruminants and rodents. Besides having been found in man in this its normal habitat, it has three times been found in various veins (the *Hexathyridium venarum* of Treutler was probably a misplaced *D. hepaticum*), and four times it is recorded as having been removed from subcutaneous tumours in which it had developed, having been carried there probably, whilst immature, in the blood. It is sometimes found in the lungs of the ox.

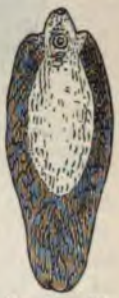


FIG. 29.—*Distomum hepaticum* (nat. size). Leuckart.

The mature parasite is a long, flat, brownish, leathery, leaf-shaped animal possessing considerable activity, and measuring from 15 to 33 mm. in length by 4 to 13 mm. in breadth. The oral sucker, which is the smaller, is placed at the top of a sort of protuberance—representing, so to speak, the stalk of the leaf; it contains the buccal orifice. A very short distance behind this is the ventral sucker, in front of which again lies the opening of the genital organs (Fig. 30). The cuticle is covered with fine spines directed backwards.

Lying in the bile-ducts the liver-fluke pours its large, brown, operculated eggs (0·13 by 0·08 mm.)—very like, but about twice the size of those of *B. latus*—into the bile. Passing out with the dung, under favourable circumstances they are carried into water where, after a variable period of from two to three weeks to as many months according to temperature, a ciliated embryo is developed. When sufficiently mature the embryo forces open the operculum, and escapes into the water. It then enters a small mollusc—*Limnæa truncatula*, or other and closely-allied species of gastropod — in the pulmonary cavity of which it passes through the sporocyst, redia, and cercaria stages of development. Finally, escaping from the intermediate host, it may encyst itself on some aquatic plant; and while in this stage, or while still in the intermediate host, or swimming, or creeping about as a free cercaria, it is transferred to the stomach of sheep or ox, and so to the biliary passages. Doubtless man becomes infected from drinking water fouled by "flukey" sheep or cattle, or from eating aquatic plants on which cercariæ had encysted themselves. The duration of the stay of the fluke in the bile-ducts is not accurately known. Some suggest nine months, others a year or longer. That they do leave the ducts spontaneously is certain, for they are sometimes passed per anum and even vomited.

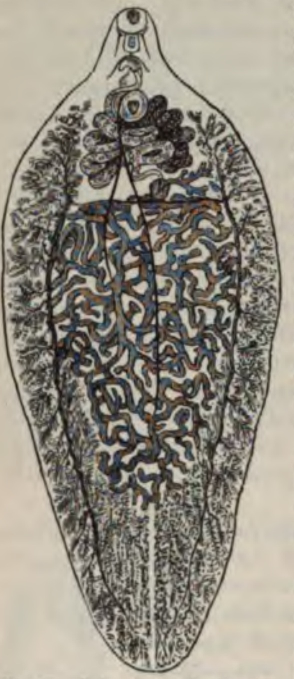


FIG. 30.—*D. hepaticum*, showing ovarian, uterine, and testicular structures (×2½). Leuckart.

In the sheep *D. hepaticum* gives rise to the important epizootic known as "sheep rot," a disease characterised by anæmia, emaciation, ascites, and œdema, and enlargement of the liver. It is very fatal, and is specially common in flocks pasturing in certain low-lying localities in which *Limnæa truncatula* and other minute gastropods abound. In some of the cases in which it occurred in man, it appears to have given rise to no particular symptoms; in other instances it has caused dilatation, thickening, and obliteration of the biliary passages, enlargement of the liver, and hypertrophy of Glisson's capsule, or even abscess of the liver. These pathological conditions were associated with a variety of symptoms, such as vomiting, diarrhœa, constipation, hepatic pains, ascites, jaundice, enlargement of the liver, fever, and so forth. In obscure hepatic affections, therefore, the vomiting or the passage of flukes per anum, or the discovery of their characteristic ova in the stools, would indicate a probable explanation of the symptoms.

Distomum lanceolatum.—This distome, which in ruminants is frequently associated with the preceding, is recorded as having been found in man five times. It is very much smaller than *D. hepaticum*. Leaf-shaped like the latter fluke, unlike this it is broader posteriorly than anteriorly. It measures from 8 to 10 mm. by 2 to 2·4 mm., is thin, supple, and devoid of cuticular spines. The dark ova (0·04 by 0·03 mm.) are provided with a double-outlined, operculated shell, and contain, even at birth, a fully-developed ciliated embryo, the cilia of which, however, cover the anterior third of the body only. The intermediate host is believed to be the mollusc *Planorbis marginalis.*

Owing to its small size this distome is not likely to damage the bile-passages seriously, and in none of the cases in which it has been found—with perhaps one exception—could it be regarded as the cause of grave hepatic trouble.

Distomum conjunctum (Fig. 31).—This parasite, discovered by Cobbold in 1858 in the bile-ducts of an American fox (*Canis fulvus*), was twice found in man, some twenty years later, by MacConnell in Calcutta. Both patients were East Indians who had died from dysentery. The distomes were present in large numbers—upwards of 100 in both cases, and lay in the dilated bile-ducts, from which they escaped on section of the liver.

D. conjunctum, in size and outline something like a flattened oat-seed, measures on an average 9·5 mm. by 2·5 mm. It is distinguishable from *D. lanceolatum* and *D. sinense* by the minute spines with which it is covered, as well as by the arrangement of its viscera. The ova have a double outline, are operculated, and measure 0·034 by 0·021 mm.

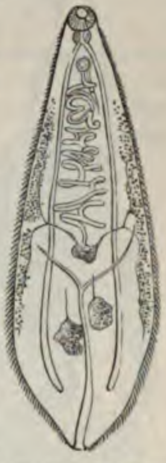


FIG. 31.—*Distomum conjunctum* (× 6). After MacConnell.

Nothing is known of its life-history; apparently it is not uncommon in the liver of pariah dogs in India.

Distomum sinense (Fig. 32)—(Synonym: *Distomum spathulatum*).—Recent investigations seem to indicate that this distome has an extended geographical distribution, that in some places it is widely endemic, and that in such places it is of considerable pathological importance. Discovered by MacConnell in a Chinaman in Calcutta in 1874, it has since been frequently found in the same race in Mauritius and in the Straits of Malacca. It has also been found in natives in Assam and in Corea. In Japan, according to Bælz, it is common in places. He describes, under the names *D. hepaticum perniciosum* and *D. hepaticum innocuum*, what seems to be this parasite, or varieties of it, as occurring in great abundance in 20 per cent of the population of certain damp, insalubrious seaside villages of the province of Okayama which have an unwholesome water-supply.

In these villages, and probably elsewhere in places in which it is endemic to a severe degree, it gives rise to a train of symptoms characterised at first by morbid hunger, epigastric weight and pain, enlargement and tenderness of the liver, and swelling of the spleen. After a few years diarrhœa, ascites, œdema of the legs, and a cachectic condition supervene; and, in the long run, lead to death. Post-mortem the liver is found enlarged, and a number of diverticula, about the size of a filbert or small nut, and containing hundreds of distomes, are discovered in association and communicating with the gall-bladder and bile-ducts. Distomes are also found free in the bile-ducts and sometimes in the duodenum. The hepatic tissue in the neighbourhood of the diseased bile-ducts is atrophied.

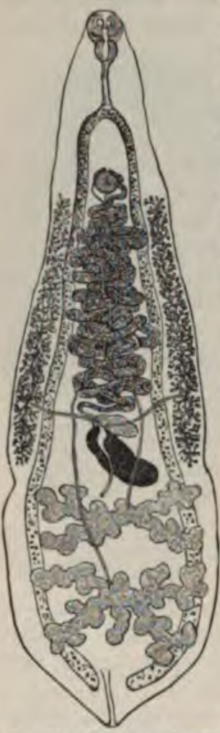


FIG. 32.—*Distomum sinense* (× 5). Leuckart.

D. sinense measures on an average 18 mm. in length by 4 mm. in breadth. Though somewhat larger, in general appearance it resembles very closely *D. lanceolatum* and *D. conjunctum*. Unlike the latter it has no epidermic spines. From the former it may be distinguished by differences in visceral structure as well as by its superior size. In *Distomum lanceolatum* the ventral sucker (0·6 mm.) is larger than the oral (0·5); in *D. sinense* the relative sizes are reversed, the oral sucker (1·0) being larger than the ventral (0·8). In *D. lanceolatum* the folds of the long and much-coiled uterine tube extend to near the posterior extremity of the helminth; in *D. sinense* they are limited to the middle part of the body, the posterior part being occupied by the large and ramified testes. Other points of difference will be readily appreciated by comparing the figures of these liver distomes. The ova of *D. sinense* are oval, granular with a double outline, and are operculated; they measure 0·03 mm. by 0·016 mm.

Further than that it is occasionally found in the cat nothing is known of the life-history of this parasite.

Distomum crassum (Fig. 33).—This, the largest of the distomes occurring in man, has been found in a considerable number of instances in Europeans living in the East, in East Indians, particularly in Chinese in Canton, Borneo, and the Straits of Malacca, and in natives of Assam and India. Recent investigations seem to show that both it and certain other and as yet unidentified distomes are by no means the rare parasites they were formerly supposed to be. Dobson, in the stools of 1249 unselected Indian coolies to whom he had administered a large dose of thymol, found large (*D. crassum*) and small (*A. hominis, D. conjunctum, D. sinense* (?)) distomes thirteen times, or in rather over 1 per cent of the cases.

In the three instances recorded by Cobbold—father, mother, and child—the parasite, which evidently had been acquired near Ningpo, China, appeared to give rise to a certain amount of intestinal irritation and to dyspeptic symptoms accompanied by irregular diarrhœa of pale stools, occasionally streaked with blood. In the other recorded instances there is no mention of any particular clinical symptom attributable to the parasite.

D. crassum is easily recognised by its great size—4 to 7 centimetres in length by 1·7 to 2 centimetres in breadth. It is thick, brown, smooth and without spines, and oblong in shape, the posterior part being somewhat the wider. The ventral sucker, which is the larger (1·6 mm.), can be readily seen by the naked eye close behind the oral sucker. The eggs are oval (0·125 mm. by 0·075 mm.), have granular contents, and are operculated. The line marking the operculum is very delicate, and is, therefore, apt to be overlooked.

The life-history of this distome is also quite unknown.

Distomum heterophyes.—This exceedingly minute distome was twice found by Bilharz in the small intestine of Egyptians in Cairo. It occurred in masses, and looked to the naked eye like minute red points. The parasitic nature of these red points was apparent on their being placed under the microscope. The individual distomes measure about 1·15 mm. in length by 0·7 mm. in breadth. They are readily diagnosed by the smallness of their size and by the character and position of the ventral sucker, which, proportionately speaking, is unusually large (0·25 to 0·35 mm.), and is located slightly in advance of the middle of the body and in front of the sexual opening. The ova (0·026 by 0·015 mm.) have a thick, reddish brown shell, the colour of which is communicated to the entire animal.

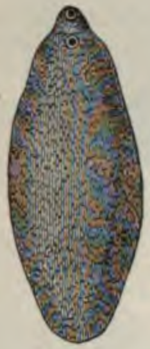


Fig. 33.—*Distomum crassum* (nat. size). Leuckart.

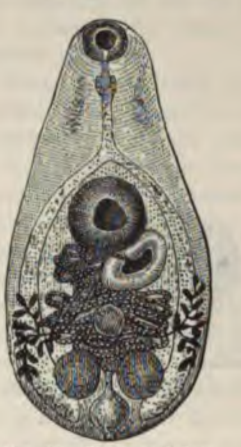


Fig. 34.—*Distomum heterophyes.* Leuckart.

Nothing is known of the life-history of this parasite, nor of any pathological condition with which it may be associated.

Distomum Ringeri (Figs. 35 and 36)—(Synonyms: *D. pulmonale*, *D. Westermanni*).—This distome is parasitic in the lungs of man in Japan, Corea, and Formosa, where, in particular districts, a large proportion of the inhabitants are affected with the peculiar form of hæmoptysis to which it gives rise. Hitherto it has not been described as occurring in man in any other region; although, seeing that it has been found in the tiger and dog, it is more than probable that its geographical range is not limited to the countries mentioned. Recently it has been found, in both the cat and the dog, in the United States. In my opinion it is a parasite of countries with a volcanic soil.

D. Ringeri is from 8 to 10 mm. in length, by 5 to 6 mm. in breadth. It is oblong in shape; very thick for a distome, being nearly circular on transverse section; leathery in consistence, and brownish red in colour. The ventral sucker, close behind which is the genital opening, is placed about the middle of the junction of the anterior with the middle third of the body. The eggs (0·08 by 0·1 mm.) are oval, operculated, brownish red, double outlined, and filled with granular contents, the embryo being not yet differentiated.

FIG. 35.—*Distomum Ringeri* (nat. size). Leuckart.

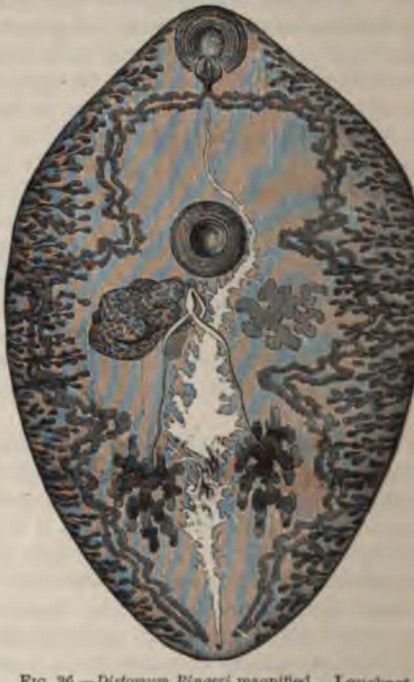


FIG. 36.—*Distomum Ringeri* magnified. Leuckart.

The mature distomes live in tunnels or burrows, with thick connective tissue walls, situated principally below the pleura near the surface of the lung. These burrows are sometimes, from the breaking down of the septa between the tunnels, converted into cyst-like cavities, which may be the size of a filbert. These cavities communicate with the bronchi by finer or larger sieve-like openings through which an ova-laden, rusty-coloured, viscid muco-pus escapes into the air-passages. This secretion excites cough and is expectorated. Several distomes may inhabit the same burrow; as many as twenty have been found in one lung. *D. Ringeri* has also been found in the cortex of the brain in two cases of a peculiar and fatal form of Jacksonian epilepsy; it has also been found beneath the peritoneum, in the orbit, and in the scrotum. It is evident that this parasite is very apt to lodge in different parts of the body and away from its normal habitat, the lungs.

The symptoms of pulmonary distomiasis are a chronic cough—usually worst in the morning, a persistent pneumonic-like sputum in which distoma ova abound, and recurring attacks of more or less profuse hæmoptysis the exact and immediate mechanism of which has not yet been explained. Little can be discovered by auscultation in the earlier stages; but in chronic cases of extreme degrees of infection signs of consolidation and perhaps of cavity may be made out. The disease lasts for many years and may prove fatal. It appears to be incurable, although I have known a case in which the patient, after many years, ceased to cough and expectorate the characteristic sputum.

In the natives of countries in which *D. Ringeri* is endemic the concurrence of pulmonary distomiasis with cerebral symptoms ought to suggest the probability that the latter are dependent on the presence of distomes in the brain. In such a case, if the symptoms are of a focal character and attributable to a cortical lesion, the propriety of removal of the parasite by surgical means might be entertained.

When the ova contained in distomum sputum are well washed and kept in a moderately warm room in fresh water, after a variable time of two to six weeks, according to temperature, a ciliated embryo is developed in their interior. On arriving at maturity the embryo escapes into the water by throwing back the operculum at the broad end of the shell. It is probable, therefore, that the intermediate host of this distome is a fresh-water animal. Beyond this nothing is known of the life-history of this important and very dangerous parasite; but this fact is of practical value as indicating the direction prophylactic measures should take.

Distomum oculi humani (Fig. 37)—*Distoma ophthalmobium.*—This was a minute and probably immature distome (1·0 by 0·5 mm.), of which von Ammon of Dresden found four specimens in the crystalline lens of a five-months-old child. Leuckart considers that they were young *D. lanceolata.*

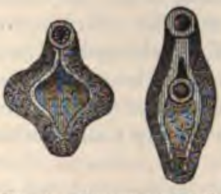


FIG. 37.—*Distomum ophthalmobium.* Leuckart.

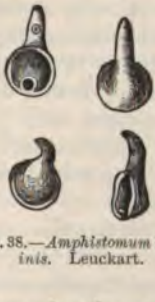


FIG. 38.—*Amphistomum hominis.* Leuckart.

Amphistomum hominis (Fig. 38).—First described by Lewis and Mac-

Connell from specimens found in an Assamese, until lately this parasite appeared to be very rare. If, however, the expression "small distomes," used by Dobson in his description of the trematodes met with during the investigations already referred to (p. 1026), applied to this parasite, it cannot be uncommon in India and similar climates. In the two cases from which Lewis and MacConnell obtained their specimens the parasite occurred in hundreds, and was found adhering with its posterior sucker to the mucous membrane of the cæcum, appendix, and ascending colon.

A. hominis is very minute, measuring only 5 to 8 mm. in length by 3 or 4 mm. in breadth at its broadest part—that is, across the posterior sucker. From the great relative breadth of the last-mentioned feature the little animal looks as if it consisted of two parts—of a disc and a short attached handle. At the end of this short handle the oral sucker is situated; between this and the posterior sucker, and on the ventral surface, the genital pore may be made out. The ova, which measure 0·15 mm. by 0·07 mm., have a firm, operculated shell.

Nothing is known of the life-history of the parasite, nor of the pathological conditions it may give rise to.

Bilharzia hæmatobia—*Distomum hæmatobium.*—See page 1091.

Class II. — Nemathelminthes. — **Order, Nematoda.** —The nematodes are long, slender, cylindrical animals with bodies which taper towards both ends, at one of which—the anterior—is placed the mouth; at or near the other—the posterior—the anus.

They are covered with a cuticle, often transversely striated and sometimes consisting of several layers. Beneath the cuticle is a cellular layer, and beneath this again a muscular layer. These three layers form the walls of a sort of tube in which lie the long straight alimentary canal, and the long and usually much convoluted ovarian, uterine and testicular structures.

The mouth is sometimes provided with papillæ, sometimes with hooks, sometimes it is simple. The short œsophagus is generally marked off from the intestine by a constriction, or by a bulb.

The female organs of generation consist of a pair of tubes, rarely of one tube only, at the upper end of which—the ovarian tubules—the germs originate; lower down fecundation is effected; lower still the germs are provided with yolk and vitelline membrane, and assume their characteristic appearance. The two uterine tubes unite to form a short vagina which opens on the ventral surface usually near the mouth, more rarely posteriorly.

The male nematodes, readily recognised by their inferior size and by their strongly curved tails, have but a single testis, a long tube filled with hat-shaped, non-flagellated spermatozoa. This opens by a vas deferens into the terminal portion of the intestine—the cloaca. In the walls of the cloaca, lodged in a sort of invagination, are usually one or two spicula—long chitinous rods which can be protracted or retracted, and serve to fix the female during copulation. In certain families the tail of the male is winged, in others it is expanded into a sort of umbrella-shaped bursa, in others, again, it is simple in structure; it is also provided, both in front of and behind the anus, with a number of papillæ. These caudal appendages form valuable marks for determining species.

Excretion is carried on by two vessels which course along the sides of the body—one on each side—in what is known as "the lateral lines." These lines are narrow, longitudinal belts in which the muscular part of the body-wall is deficient. The two vessels they include unite anteriorly and open by a transverse slit—the vascular pore—on the ventral surface.

Unlike what occurs in the cestodes and trematodes, the sexes in the nematodes are, with few exceptions, separate, though very generally they live in association.

Usually oviparous, not a few are viviparous or ovo-viviparous. The embryo is a long, slender, cylindrical, eel-shaped organism which, while *in ovo*, is coiled up, but when free is outstretched and exhibits active movement. Sometimes it gets access to its definitive host directly; usually, however, it has first to pass through a metamorphosis in an intermediate host. Certain species possess what is known as the "free rhabditis form" and are heterogamous; that is to say, the embryo emanating from the parasitic form becomes sexually mature as a free form, and has young for one or more generations before its descendants revert to the parasitic condition.

Family—Ascarida

The members of this family of nematodes are characterised by their comparatively stout bodies, and by the possession of three well-marked lips carrying papillæ—one lip being dorsal, the other two being ventral and meeting in middle line. The tail of the male is strongly curved and carries two spicules. Three species are parasitic in man.

Ascaris lumbricoides (Fig. 39) (Synonym: Round worm), whose usual and normal habitat is the upper part of the small intestine, is, with one rare exception, the largest of the nematodes parasitic in man. The male worm measures 15 to 25 cm. in length by 4 mm. in breadth; the female 16 to 45 cm. by 6 mm. Both are cylindrical in shape, and taper to the ends particularly towards the head. Close to the tail the body is somewhat flattened in a ventro-dorsal direction. In colour they are gray or pinkish; to the touch they are firm and rigid. The surface is glistening and

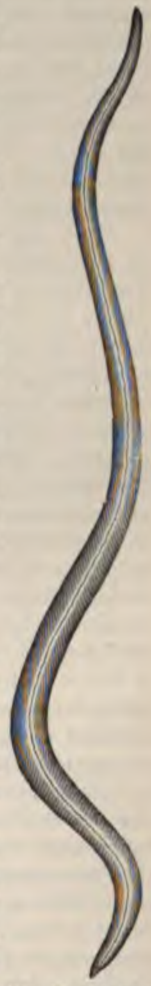


Fig. 39.—*Ascaris lumbricoides*, female (reduced).

polished, and is marked by fine, closely-set, transverse ridges. The musculo-cutaneous body-wall is so transparent that the coils of the long uterine or testicular structures can be discerned through it in many places. The tail of the female, close to the tip of which opens the two-lipped, transversely disposed, slit-like anus, is straight. That of the male is strongly curved in a ventral direction, two spicules usually protruding from the subterminal cloaca. On the ventral surface of the tail, and extending as far as the curve extends, some 69 to 75 minute papillæ are arranged on both sides of the middle line. The two much convoluted uterine tubes are of great length—ten to fifteen times that of the worm—and occupy the posterior two-thirds of the body. They unite to form a short vagina which opens ventrally some distance behind the head. The excretory canals, lying in the lateral lines, unite and open a short distance behind the mouth. The three papillæ-bearing lips characteristic of the family are very well marked.

The ova (0·075 mm. by 0·058 mm.), of which the uterine tubes contain many millions, are ovoid, spherical, or sometimes barrel-shaped. They have a rough mammillated surface, a multiple outline, and granular contents. White while in the uterus of the worm, they are stained brown by the bile on entering the intestine of the host. At birth, and for a long time afterwards, they exhibit no sign of the embryo; but if kept in water, in the light, and at a summer temperature, an embryo of the usual nematode character is developed in the course of five or six months. Some experimentalists state that during the heats of summer the embryo may be developed in a couple of weeks. Desiccation in summer and freezing in winter suspend development, but kill neither ovum nor embryo. When fully developed the embryo still remains in the egg and does not seek to escape spontaneously. It will remain alive under suitable conditions for upwards of five years. On the ovum being swallowed by the definitive host, the embryo speedily breaks through the shell and advances so rapidly in development that at the end of a month it is a sexually mature animal giving birth to crowds of ova. These facts have been proved by carefully-conducted feeding experiments. Von Linstow's suggestion, that a certain myriapod—*Iulus guttulatus*—acted the part of intermediate host, seems therefore to be superfluous.

Ascaris lumbricoides is cosmopolitan, being found in all countries from the arctic circles to the tropics. In a general way it may be said to be much more common in the tropics than in cooler latitudes; a great deal depends of course on local conditions, particularly on the character of the water and vegetable supplies, and their liability to contamination by fæcal matter containing the ova of the parasite. As a rule it is more frequent in the country than in towns, in children and young people than in adults or infants. It has been found, however, in infants only 11 weeks old, and in old age up to 78. Lunatics, doubtless owing to their careless or filthy habits, are particularly subject to ascarides.

In temperate climates one, two, or up to ten may be found together in one host; but in the tropics twenty or thirty are not uncommon, and instances of hundreds being found in the same patient are far from rare. Perhaps the most remarkable case on record is one published by Fauconneau-Dufresne, in which a boy of 12 passed over 5000 worms in less than three years—most of them by vomiting; 600 were got rid of in a single day.

Although the small intestine is the usual seat of these worms, not infrequently they wander downwards into the large intestine or upwards into the stomach, and so into the œsophagus, and out by the mouth or nostrils. They have even caused death from suffocation by creeping into the glottis. Cases are on record in which they had entered the Eustachian tubes or the nasal ducts, finding their way to the outside by the external ear in the one case, or by the canaliculi lachrymalis in the other. A more frequent occurrence is their impaction in the biliary or pancreatic ducts; in these situations sometimes several worms have been found together. Thus located they may give rise to grave symptoms from blocking and dilatation of the ducts; even abscess of the liver has resulted from such an invasion. In other cases, by perforating the intestine round worms may escape into the peritoneal cavity, setting up peritonitis; more especially if some of the intestinal contents escape along with the worms. In some instances peritonitis has not ensued; in the latter cases, and also in many of the cases in which these worms were found at the post-mortem examination in the air-passages, it is not improbable that the wandering did not take place till after the death of the host. This post-mortem wandering may be correlated to the curious fact that in acute disease, and as death approaches, round worms often exhibit a disposition to quit the patient's body. There have been many instances of verminous abscess recorded, particularly as affecting the umbilical region in children and the groin in adults, which were most probably connected with the imprisonment of ascarides in hernial protrusions of the bowel. Kidney, spleen, pleura, and the urinary passages have sheltered strayed specimens of these parasites at times; they have even escaped by the urethra.

Symptoms.—From the fact that in many countries scarcely an individual up to middle life is free from this parasite, it is manifest that *Ascaris lumbricoides* does not necessarily or usually give rise to important pathological conditions. Nevertheless, there are good grounds for believing that at times, particularly in young children and in others with sensitive nervous systems, it is really a cause of more or less grave reflex or direct disturbance. Thus it appears to be an occasional excitant of convulsive seizures; of perversions of the senses of sight, smell, hearing, and taste; of vertigo, hysteria, mental disturbances, dreams, and so forth: at all events, in many such cases these morbid symptoms have disappeared on removal of the parasites. Such direct effects of its presence in the alimentary canal as dyspepsia, griping pains, nausea, vomiting, irregular action of the bowels, mucoid, membranous, or bloody stools, excessive, defective, or perverted appetite, itching of the nose or anus, malnutrition and anæmia are very common in association with this parasite; they subside at once on the successful action of an anthelmintic.

Diagnosis.—Failing the spontaneous discharge of a lumbricus in the stools or in vomited matters, a dose of santonin will quickly confirm or negative any suspicion of their presence. When it is deemed inadvisable to give this drug on bare suspicion, a microscopic examination of the stools will clear up the diagnosis at once. In cases of ascaris infection the number of ova is so prodigious that the minutest portion of fæces is nearly sure to contain several specimens. To examine it, all that is necessary is to express a small portion, not larger than a big pin's head, between a cover-glass and slip, and to search every part of it with a magnifying power of something under 100 diameters. If the stools be fluid they should be allowed to stand, and the sediment then examined.

Treatment.—Round worms are got rid of at once by the administration of santonin. It is best to combine it with a purgative. A few grains of calomel or a dose of castor oil suffice. A good plan is to give half a grain to four grains, according to age of patient, for three successive nights at bed-time, and on the mornings following the first and third doses to exhibit a dose of castor oil. In the tropics, and in countries in which the parasite is particularly prevalent, such a course of santonin may be administered to children twice a year with great advantage to their general health. When prescribing santonin the physician should warn the patient or, in the case of a child, the attendants of the effect of this drug in causing temporary discoloration of the urine—a greenish yellow tint in acid, a red or purple tint in alkaline urine. He should also inform them of the effect on vision—objects appearing some hours after the dose of a blue and, later, of a yellow colour; and perhaps, finally, there may be temporary loss of colour vision. Rarely does a medicinal dose give rise to serious toxic symptoms such as asphasia, tremors, hallucinations, convulsions, enfeebled respiration, slowing of the pulse; though sometimes this occurs after santonin: in particular idiosyncrasies unnecessarily large doses must therefore be avoided.

It is manifest, from what has been said about the life-history of the parasite, that a pure water-supply is the best prophylactic. Where this cannot be secured all drinking-water should be boiled. Similarly, wherever the nature of the fertilisers employed by market gardeners is not beyond suspicion, all vegetables should be cooked or well washed in boiled water.

Ascaris mystax (Fig. 40).—Normally parasitic in dogs, cats, and some other carnivora, this species is sometimes found in man. It can be readily recognised by its relatively small size (male 4 to 6 c.m. long, by 1 mm. in diameter; female 6 to 12 c.m., by 1·7 mm.), by the two very conspicuous cutaneous wings projecting from each side of the head in both sexes, giving the head end a cordiform or arrow-head appearance, and by the number and arrangement of the four pairs of pre-anal and three pairs of post-anal papillæ on the tail of the male. The ova (0·068 by 0·075 mm.) are covered with a beautiful net-work something like the mace on a nutmeg.

Oxyuris vermicularis (Fig. 41) (Synonyms: *Ascaris vermicularis*, Thread worm, Seat worm), like *A. lumbricoides*, is a very common parasite and is found in all countries. Like the round worm it has a predilection for children and young people, in whose fæces they are by no means an infrequent feature, looking like minute (9 to 12 mm. long by 0·4 to 0·6 mm. broad), white, slowly moving, short pieces of fine thread. These are the female oxyurides. The male worms, which are both fewer in number and very much smaller (3 to 5 mm., by 0·16 to 0·20 mm.), are hard to find in the stools or intestinal mucus without the aid of a lens. The sexes are further distinguished by their tails—that of the female being long, tapering, and pointed, the anus opening at its base; the vagina opens on the ventral surface a little in front of the middle. In the male the tail is abruptly truncated; usually, particularly after death, it is coiled up into a sort of spiral; the cloaca is terminal and contains only a single spicule; the tail is further distinguished by six pairs of ventrally placed papillæ, of which the anterior and the posterior pairs are the largest. In both sexes the head end is very much pointed, and carries on its upper and under aspects a peculiar cuticular bag filled with clear fluid. Viewed in profile this double bag or crest gives the head an appearance which is very aptly compared by Blanchard to the amber mouth-piece of a Turkish tobacco pipe.

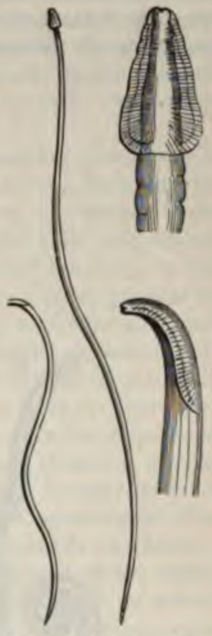
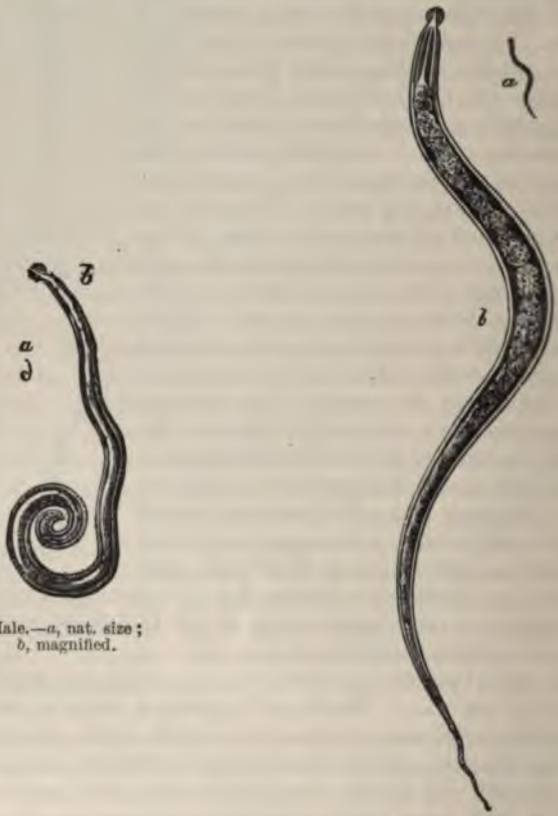


FIG. 40.—*Ascaris mystax.*

The eggs (0·05 by 0·016 to 0·024 mm.) are oval, but much flatter on one side than on the other. Their shell consists of three layers, except at one point on the dorsal surface where the middle layer is defective. It is at this point that the embryo subsequently effects its escape.

At the time the egg leaves the parent worm the embryo, though visible, has not quite completed its intraoval development. So soon, however, as the ovum enters the fæces, whether inside or outside the host, progress is rapid; but until transferred to the human stomach the development of the embryo does not advance beyond a certain point, the little animal always remaining a prisoner in the shell. Under suitable conditions it remains alive in this state for days or weeks. Long immersion in water is said to kill it; consequently, we may infer that the drinking-water is not a usual medium of infection with oxyurides. An intermediate host is not required. The ova get access to the human stomach on fruit, raw vegetables, in dust, by being conveyed on dirty fingers to the mouth, and probably in many other and similar ways. When ova or pregnant oxyurides are swallowed experimentally, mature worms appear in the fæces at the end of two or three weeks. Grassi, after swallowing six female oxyurides, found their progeny in his stools at the end of fifteen days; and they continued to appear in every stool for over a month. From the latter circumstance it is evident that development does not proceed in all the ova, nor probably in all the worms, simultaneously.



Male.—*a*, nat. size;
b, magnified.

Female.—*a*, nat. size;
b, magnified.

Fig. 41.—*Oxyuris vermicularis.*

It is believed that on the egg being swallowed the embryo is liberated in the stomach; it then passes into the small intestine, where, after undergoing a succession of moultings, it attains sexual maturity and impregnation is effected. The male worm usually dies after this event, passing out in the fæces; but the impregnated female migrates to the cæcum, where she remains till her ova are matured. She then descends to the rectum, where part of her ova are probably expelled, she herself perhaps passing out along with them in the fæces. Other worms escape spontaneously by wriggling through the anus, and, doubtless aided by the scratching and manipulation their presence occasions, spread over the neighbouring integument, and even wander into vagina, urethra, or prepuce. Thus they scatter their eggs about, and by their movements cause intolerable itching. The warmth of bed seems to provoke this exodus of oxyurides; for it is usually on going to bed that the characteristic migration and attendant irritation set in, phenomena which recur with remarkable regularity and at the same hour every evening.

The irritation secures by auto-infection the continuation of the race of animals producing it. By the scratching that ensues, the wandering worms are broken up, and their eggs, and even fragments of the worms themselves, are smeared over the fingers, forced under the nails, and spread about the body. In this way the eggs are inadvertently conveyed to the mouth of the host, to be swallowed and so to start a fresh generation of parasites. The itching of the nose, which is so frequent a concomitant of rectal and intestinal irritation, and such habits, so common in children, as sucking of the thumbs during sleep and biting of the nails, contribute to ensure this result. In this way patients keep up their stock of parasites for many years, and often into adult life. In some instances the intestines have been so loaded with these worms that the mucous membrane looked as if covered with a pile like velvet. Usually infection does not proceed to this degree; but thousands of worms are often present in the bowel, agglutinated by the mucus into masses and balls.

Symptoms.—In consequence of the nocturnal wanderings of the worms and the intense irritation they give rise to, local symptoms, such as mucoid and bloody stools, morbid sexual excitement leading to masturbation, seminal emissions or enuresis, eczematous conditions about the anus, and pains resembling those of stone in the bladder, are common. Reflex disturbances may also occur, such as hysteria, convulsions, chorea, perversions of appetite, anæmia, and similar consequences of prolonged intestinal irritation. In the presence of such symptoms the appearance of worms or ova in the stools at once establishes the diagnosis.

Treatment.—The facts of the life-history of the parasite, as just set forth, must be borne in mind in directing treatment. Grassi's experiment has shown that the parasites may continue to arrive at maturity in successive swarms during the last four or five of the six or seven weeks following a single infection. Consequently, treatment to be radical must extend over this period at least. Moreover, measures must be taken to prevent auto-infection. With this latter object in view, in the case of a child care should be taken that the buttocks are covered with stout drawers during sleep; or a long night-dress may be tied beyond the feet, or some such device employed so as to make it impossible for the child to soil the fingers with the ova of such worms as may creep out from the anus during the night. It is a good plan to cover the hands with gloves. Finger-nails must be kept short and clean, and thumb-sucking and nail-biting discouraged. An affected child should sleep by itself, so as to minimise the risk of spreading the complaint.

An occasional aperient had better be administered during treatment. Every night for a time, and later every second or third night, an anthelmintic enema must be administered. There are many efficient drugs which may be employed in this way. Salt and water, an ounce to the pint, infusion of quassia, a few drops of tincture of the perchloride of iron, vinegar or alcohol and water, and lime water may be mentioned. As it is hopeless to reach the cæcum, where the bulk of the worms is situated, by enemas, such means are of use only in killing or dislodging those parasites which have descended to the rectum prior to their escape per anum; the enema therefore need not exceed a pint in the adult or five ounces in the child. Suppositories of quassia with coco butter are said to be an efficient and convenient substitute. If precautions are effectually taken against reinfection from without, and auto-inoculation, the worms disappear rapidly; and a radical cure may be looked for in from four to six weeks. Nocturnal irritation is prevented by smearing the neighbourhood of the anus with weak mercurial ointment, or sponging with carbolic lotion.

In families and large public institutions in which this helminthiasis has broken out some trouble should be taken to prevent its spread. Particular care should be exercised to secure clean underclothing, clean bed-linen, clean towels, and clean privies; raw fruit and vegetables should be interdicted, and all plates, dishes, and drinking-vessels so cared for that such dust or dirt as might possibly contain ova of the parasite is prevented from contaminating them.

Ascaris maritima.—Only one immature specimen has hitherto been found. It was vomited by a child in Greenland, and has been described by Leuckart.

Family—Strongylida

In the *Strongylida* the male opening is placed at the posterior end of the body at the bottom of an umbrella or bell-shaped copulatory bursa, the margin of which is furnished with a varying number of papillæ.

Eustrongylus gigas—(Synonyms: *Strongylus gigas*, *Eustrongylus visceralis*, Giant strongyle).—This, the largest of the nematodes affecting man, is much more frequently found (although even in them it is by no means a common parasite) in certain other mammalia—particularly, according to Leuckart, in those that are always or occasionally ichthyophagous, such as the dog, wolf, fox, and seal. It has also been found in the ox and horse, which, as is well known, in northern latitudes sometimes eat fish. It is conjectured that certain larval nematodes of the muscles of fish are an early stage of this parasite; experiment has not confirmed this conjecture.

In appearance the giant strongyle is like an overgrown *A. lumbricoides*; it is readily distinguished, however, from this parasite by its enormous size, and by the copulatory bursa on the tail of the male, which is so large as to be quite apparent to the naked eye. The male measures from 14 to 35 c.m. in length by 4 to 6 mm. in breadth; the female 25 c.m. to 1 metre in length by 4·5 to 12 mm. in diameter. The male has only one spicule, which protrudes from the cloaca at the bottom of the copulatory bursa. The eggs are oval (0·064 mm. to 0·068 mm. by 0·042 to 0·044 mm.), and have a thick, brown, fragile, foveolated shell which is quite characteristic and constitutes an important diagnostic indication if met with in bloody urine.

The parasite is usually located in the kidney. Two or three or more may be found together; in rare cases even as many as eight. Sometimes it appears to cause little damage and few symptoms; more usually it causes disorganisation of the organ, converting it into a pus-filled cyst, and giving rise to much pain and hæmaturia. It may leave the kidney and stray to the peritoneal cavity, to the pleura, to the liver, bladder, perinephritic fascia, and other parts, in which situations it has been occasionally encountered in the lower animals. Although it has only been found some six or seven times in man, it has a wide geographical distribution, having been met with in the lower animals in most countries of Europe, and of North and South America.

Should the characteristic ova be found in the urine, and local pain determine the kidney in which it is located, the parasite might be removed by surgical means.

Strongylus longevaginatus.—This parasite has only been once found, and then in large numbers, in the lungs of a boy in Transylvania. The males measured 15 to 17 mm. in length by 0·55 in diameter, the females 26 mm. by 0·7. This species is probably allied in habit to the various strongyles which affect so frequently the air-passages of many of the lower animals.

Ankylostomum duodenale (Fig. 42)—(Synonyms: *Anchylostoma duodenale*, *Anchylostomum duodenale*, *Dochmius duodenalis*, Tunnel worm).—Since Dubini discovered this parasite in Milan in 1838 it has been found in so many countries that it is highly probable that *A. duodenale* is generally endemic all over the globe between the parallels 51° 31′ N. and 30° S.; at all events in those localities where the character and hydraulic conditions of the soil and the habits of the inhabitants favour its propagation. In Egypt it is found in nearly every cadaver; in India, Dobson found it in the stools of 75·58 per cent of 1249 natives to whom he had administered thymol. It seems to be equally common in the West Indies, Guiana, Brazil, Java, Ceylon, the Straits Settlements, Java, Japan, and, indeed, in most other tropical and subtropical countries in which it has been searched for. I have seen its ova in the stools of Indian Lascars in England, but, according to Cobbold, it is not endemic in this country. It is frequently met with in the warmer regions of Europe and of North America.

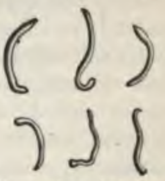


FIG. 42.—*Ankylostomum duodenale* (nat. size). After Schulthess.

The normal habitat of *A. duodenale* is the small intestine of man, particularly the jejunum; less often the duodenum, rarely the ileum or lower reaches of the alimentary canal; occasionally it has been found in the stomach. In these situations it attaches itself by means of its powerful buccal armature to the mucous membrane, from the blood of which it obtains a plentiful supply of nourishment. It is supposed to shift its hold from time to time, the abandoned bite oozing blood for a little while. It is further said to be very prodigal of the blood it imbibes, the red corpuscles passing through its alimentary canal unchanged, the plasma alone being utilised.

The male and female ankylostoma—present generally in the proportion of one of the former to three of the latter—do not differ so much in size as do many of the other nematodes. The males measure from 6 to 11 mm. in length by 0·4 to 0·5 mm. in breadth; the females 7 to 15 mm. in length by 1 mm. in breadth. Both sexes are cylindrical in form; white when they are alive, gray when dead, or reddish brown when full of blood. In both sexes the posterior end is the broadest part, whence the body tapers forward to a narrow neck, which ends in the bulging and distinct mouth capsule. The margin of this remarkable organ is furnished with four strong, claw-like hooks—two on each side of the ventral line, and two conical teeth—one on each side of the dorsal line. The tail of the female is conical and ends in a short, delicate spine, the anus being subterminal and the vagina opening on the ventral surface at the commencement of the posterior third of the body. The tail of the male is provided with a large umbrella-like trilobate bursa, having eleven ribs; two long and delicate spicules project from the cloaca at the bottom of the bursa. Owing to the relative positions of the sexual openings the worms in conjugation look like the Greek "γ."

The female ankylostoma produces a prodigious and never-ending stream of eggs which passes out in the fæces of the host. These eggs (0·055 to 0·065 mm. by 0·032 to 0·043 mm.) have a regular oval form, with a delicate, smooth, and beautifully transparent shell, through which the grayish and distinctly segmented yolk can be readily seen. While in the body of the host development does not advance further; but on leaving it development proceeds, under suitable circumstances, so rapidly that in one to two days a rhabditiform embryo (0·2 mm. by 0·014 mm.) is born. This minute organism is very active, voraciously devouring what organic matter it can find, and for a week it grows very rapidly (to 0·56 mm. by 0·024 mm.) During this time it moults twice. After the second moulting it passes into a sort of larval state during which it no longer eats and growth is suspended. In this condition it may live for weeks or months, moving about more or less languidly in muddy water, in mud, or in damp earth. Should chance so determine, it is finally transferred to the human alimentary canal either in muddy drinking-water, or in the mud or dirt adhering to the hands or dishes of the agriculturist, the brickmaker, or other operative engaged in handling the soil; or, it may be, in earth deliberately eaten by the geophagist. Arrived in its final host, after moulting again at the end of five weeks (Leichtenstern), it acquires sexual characters and the permanent adult form. The duration of the life of *A. duodenale* in the intestine has not been determined; some state it in months, others in years (Sonsino).

Giles holds that *A. duodenale* may become sexually mature while outside the body and in the free state; in other words, that it is heterogenetic. His observations have recently been confirmed in part by Sandwith, but doubt has been thrown on their relevancy by Sonsino and Macdonald.

Ankylostomiasis.—Such is the life-history of this parasite, so far as is known. Considering its insignificant size it is unlikely, so long as its numbers are small, that serious inconvenience should result from its presence in the intestine; but when these numbers mount up to hundreds or thousands, as is often the case, the constant drain of blood they keep up for months or years, the dyspepsia and malnutrition entailed by their presence, and the wounds they inflict on the mucous membrane bring about a grave cachexia—the state known as ankylostomiasis—which not infrequently leads to a fatal issue.

The recognition of this form of helminthiasis as an important pathological condition is of comparatively recent date. Griesinger was the first to point out that the form of anæmia known as Egyptian chlorosis is of this nature; and, later, other observers showed that a similar anæmia was common among negroes in America. Public attention, however, was not forcibly directed to the subject until 1880, when the occurrence of the notorious epidemic of anæmia among the workmen engaged in making the St. Gothard Tunnel was shown to be of this nature. It was subsequently discovered that similar anæmic conditions, originating from the same cause, were not uncommon among the workmen employed at certain European mines; and recently it has been proved that the parasite and the cachexia to which it gives rise are exceedingly common in Africa, in India, and, indeed, all over the East.

As with many discoveries, on their first being made known the importance of the ankylostomum was much exaggerated, not a few diseases—beriberi, for example—being attributed to it, with which it is in no way concerned. Nevertheless, although many of the diseases for which it has been blamed have nothing to do with the ankylostomum, it cannot be doubted that this parasite in many instances well deserves the evil reputation it has acquired.

The exact conditions under which *Ankylostomum duodenale* becomes gravely pathogenetic are perhaps not yet thoroughly understood, for we meet with all the symptoms of pronounced ankylostomiasis in patients whose intestines contain comparatively few ankylostomes; whereas these parasites may be present, even in vast numbers, in persons who are, notwithstanding, to all appearance healthy and robust. In determining the establishment of this cachexia much must depend, therefore, upon individual idiosyncrasy in respect of digestive powers, the tolerance of blood depletion and of intestinal irritation; also on the individual physiological margin, on the conditions of physical work, and on the quantity and quality of aliment obtainable. It can be readily understoo

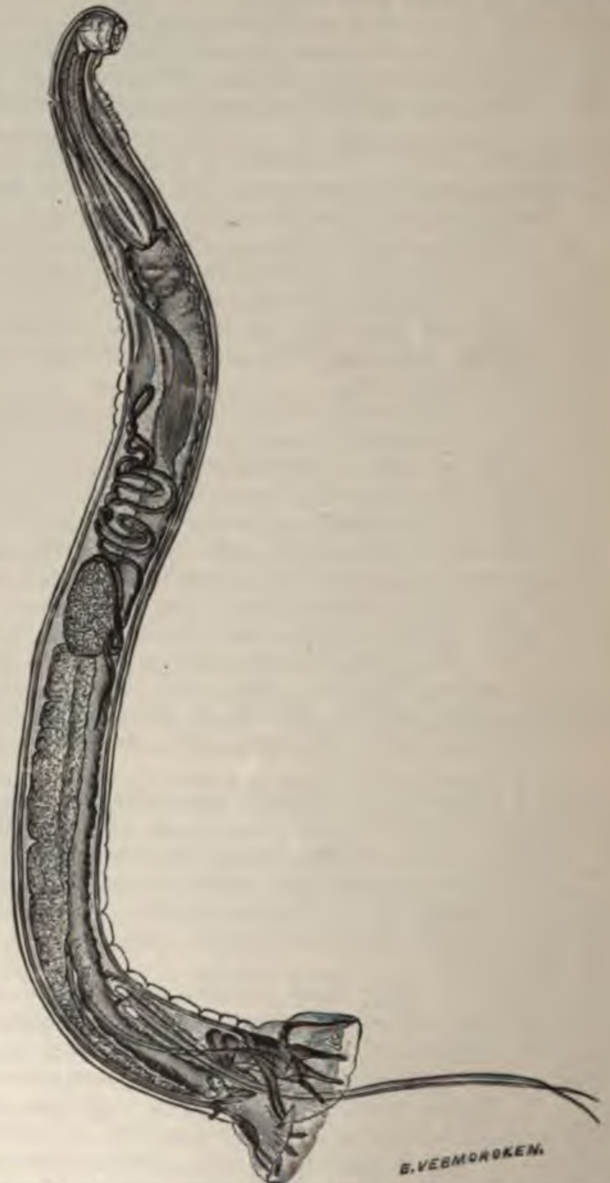


Fig. 43.—*Ankylostomum duodenale*, male (highly magnified). After Schulthess.

that a vigorous, healthy European, well nourished on flesh, eggs, and suc

like concentrated and easily digested foods, will stand a larger invasion of ankylostoma than the feeble, limp, labouring Indian. The latter, to obtain sufficient nutriment from his coarse dietary of sweet potatoes, rice, vegetables, and other bulky and innutritious foods, has so to stuff his stomach three or four times a day that dilatation of that organ, and the various catarrhal and dyspeptic conditions thus entailed, must necessarily ensue; doubtless these concomitants have a large share in the production
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in the stools. Temperature is usually subnormal; at times there may be transient flashes of fever.

As the disease advances signs of anæmia set in—such as pallor of mucous surfaces and complexion, breathlessness, lassitude, palpitations, hæmic bruits, tinnitus, dimness of vision, vertigo, depression and apathy, irritability of the circulation, attacks of syncope, œdema of the feet, and the usual train of symptoms attending recurring and prolonged hæmorrhage. Hæmocytometric observation shows a fall in the corpuscular richness of the blood—perhaps to one million per cubic millimetre—the hæmoglobin value of the individual corpuscles being fairly maintained. Retinal hæmorrhages have also been observed.

Secondary dyspeptic conditions, such as gastralgia, vomiting, hæmatemesis, dilatation and ulceration of the stomach, often complicate and quantity and quality of aliment obtainable. It can be readily understood

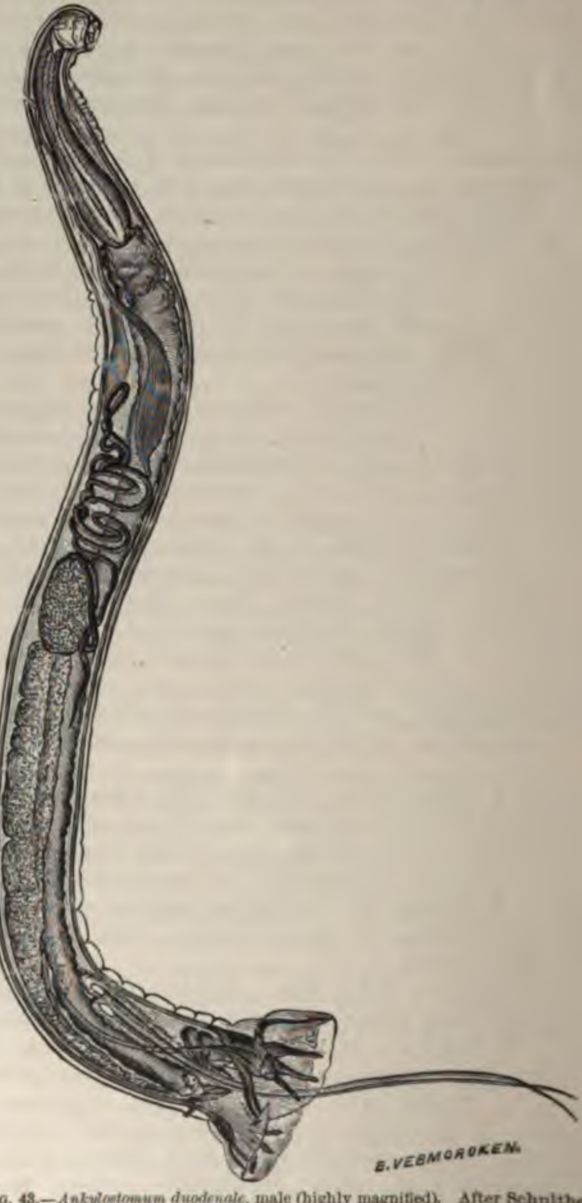

FIG. 43.—*Ankylostomum duodenale*, male (highly magnified). After Schulthess.

that a vigorous, healthy European, well nourished on flesh, eggs, and su like concentrated and easily digested foods, will stand a larger invasion of ankylostoma than the feeble, limp, labouring Indian. The latter, to obtain sufficient nutriment from his coarse dietary of sweet potatoes, rice, vegetables, and other bulky and innutritious foods, has so to stuff his stomach three or four times a day that dilatation of that organ, and the various catarrhal and dyspeptic conditions thus entailed, must necessarily ensue; doubtless these concomitants have a large share in the production of the pathological picture in which the ankylostomum is only one, though perhaps the leading feature.

Then, again, in many tropical countries a considerable proportion of the population lives in a chronic state of semi-starvation hard for us to realise. Under such conditions the daily loss of blood which a few hundred ankylostomes entail is a serious matter, and may be all that is required to turn the scale and start the vicious circle of famine degenerations.

Symptoms.—The essential symptoms of ankylostomiasis are those of a progressive anæmia associated with symptoms of intestinal catarrh leading in time, if not checked, to fatty degeneration of the heart and other organs, and ultimately to serous effusions and death.

Pain in the epigastrium radiating towards the umbilicus, increased by pressure, but generally relieved by food, is one of the earliest signs of invasion by ankylostoma. This pain may be accompanied by dyspeptic troubles, colicky symptoms and borborygmi. The appetite is very often ravenous, although the digestive powers may be feeble; occasionally there is anorexia. Perverted appetite—pica or geophagy, as it is sometimes called—is a common occurrence in this as in other forms of intestinal helminthiasis, and is especially dangerous in ankylostomiasis, as in this malady its indulgence tends to accumulate the infection. The bowels, generally constipated at first, may in the advanced disease be loose and irregular. Sometimes, though rarely, the stools have a reddish brown tinge from sanguineous admixture, and pieces of blood-tinged mucus may be passed; but pure blood is rarely seen, for, though escaping perhaps in considerable quantity from the wounds made by the parasites in the upper part of the intestine, it is so mixed with the chyme, and so altered by the intestinal juices, that it is not recognisable in the stools. Temperature is usually subnormal; at times there may be transient flashes of fever.

As the disease advances signs of anæmia set in—such as pallor of mucous surfaces and complexion, breathlessness, lassitude, palpitations, hæmic bruits, tinnitus, dimness of vision, vertigo, depression and apathy, irritability of the circulation, attacks of syncope, œdema of the feet, and the usual train of symptoms attending recurring and prolonged hæmorrhage. Hæmocytometric observation shows a fall in the corpuscular richness of the blood—perhaps to one million per cubic millimetre—the hæmoglobin value of the individual corpuscles being fairly maintained. Retinal hæmorrhages have also been observed.

Secondary dyspeptic conditions, such as gastralgia, vomiting, hæmatemesis, dilatation and ulceration of the stomach, often complicate and aggravate the case at this stage. Yet, strange to say, with all this anæmia and the secondary dyspeptic conditions, provided the feeding be good and sufficient, the patient remains fat and plump; the intense pallor and œdema are the only objective symptoms which force themselves on the attention.

Progress is sometimes very rapid; in a few weeks the patient may be brought to a dangerous state of anæmia, and even death may occur from syncope or serous effusions. The vast majority of cases, however, have a more chronic course, extending over years; in these, if death result, it is often due to some intercurrent disease.

In children, not only does the ankylostomum produce anæmia, but it stunts the growth and delays the occurrence of puberty. When such children grow up—particularly if malarial cachexia be combined with ankylostomiasis—they remain childish in appearance, puny in size, sexually immature, and with characteristic high-pitched treble voices.

Diagnosis.—The secret of the diagnosis of ankylostomiasis, like that of so many other diseases, is to suspect its presence. Microscopic examination of the fæces justifies or dismisses this suspicion at once. If ova are found, some idea of the extent of the infection may be got from an enumeration of the eggs in a given quantity of fæces. According to Grassi and Parona, 150 to 180 eggs per cubic centigramme of fæces indicate approximately an infection of 1000 worms, male and female together. Sometimes it happens that although the ankylostoma have disappeared, the subsequent anæmia and degenerations progress, even to a mortal issue; the fatal pathological circle of famine changes having become established before the worms had been got rid of. In these cases ova are, of course, absent from the stools, and a diagnosis can only be guessed at from a consideration of the history and other circumstances. On the other hand, although a certain number of ova may be met with in the stools of some cases of anæmia, the diagnosis of ankylostomiasis must not be jumped at without a careful consideration of the entire circumstances of the case, and a careful exclusion of such causes of anæmia as malarial disease, Bright's disease, cancer, tubercular disease, pernicious anæmia, leucocythæmia, and so forth. It should always be borne in mind that the majority of the natives in many warm countries harbour ankylostoma and trichocephali besides the more readily recognised *Ascaris lumbricoides*; and that, therefore, the presence of any or all of these parasites may be expected in many diseases for which they are not in the slightest degree responsible.

The pathological anatomy is that of extreme anæmia, plus the local lesions in the small intestines produced by the ankylostomes. Besides the extreme pallor and bloodlessness of all the tissues, there is general œdema, and often also effusion into the serous cavities. Many of the viscera show signs of fatty degeneration, particularly the heart, which is pale, yellowish, flabby, and dilated. Some pathologists claim to have found an excess of iron in the liver, pointing to a hæmolytic as well as a simple hæmorrhagic origin for the anæmia; such a hæmolysis they attribute to the absorption by the intestine of some product of the parasite. Other observers deny any excess of iron in the liver, and, consequently, the toxic absorption referred to. If careful search be made soon after death in the small intestine the ankylostoma may be found still attached by their mouths to the mucous membrane; if the post-mortem has been delayed the parasites will be found loose in the mucus. Scattered about the intestine, in and under the mucous layer, and showing through the serous and muscular coats of the pallid bowel, a number of small ecchymoses are to be seen. If the centres of these be carefully scrutinised the minute wound inflicted by the ankylostome can be detected. In rare instances parasites have been found, singly or in pairs, in a blood-filled cavity the size of a filbert underneath the mucous membrane; a minute aperture, the hole by which the worms had entered, opening into it. The sites of old hæmorrhages are indicated by punctiform pigmentation. At times there may be thickening and even swelling of the mucosa and other signs of old and recent catarrh. The mucous membrane of that part of the bowel where the parasites are located is usually streaked with blood; rarely (although such cases are on record) is the bowel found filled with a more extensive hæmorrhage.

Treatment.—Until the introduction of thymol by Bozzolo in 1880, the extract of male fern, in heroic and sometimes toxic doses, was the only efficient anthelmintic in ankylostomiasis. In Brazil the juice of the *Ficus dolearia* enjoyed a certain reputation. Both of these remedies have now been superseded by thymol, which seems to have the further advantage of being effective against a variety of intestinal parasites, such as tapeworm, *D. crassum*, *A. hominis*, and possibly others.

To be effective thymol must be given in full doses, 15 to 30 grains, repeated four times at intervals of one and a half to two hours. If the bowels do not act spontaneously within twelve hours of the last dose a purgative should be given. It is well to clear out the bowels the day before the administration of the thymol, and to place the patient for the time being on liquid diet.

The drug is best administered in cachets or tabloids. In hospital or dispensary practice in the endemic districts considerations of expense suggest that it had better be given in suspension, care being taken that it is finely triturated before mixing. A draught may be served out from a stock-bottle so prepared.

Although thymol is very insoluble in water there is some danger attending its use and arising from its absorption in poisonous amount. One precaution must be taken against such a mishap. Thornhill of Ceylon, as well as others with extensive experience in the use of the drug, state this most emphatically, and refer to several deaths from collapse after full doses. Thymol is very soluble in alcohol, ether, turpentine, chloroform, oil, certain alkaline solutions, and in glycerine. Therefore, during treatment, and while the drug is still in the alimentary canal, these solvents must be carefully withheld. These dangers and precautions are, as a rule, not sufficiently recognised by practitioners, nor insisted on by authors. Signs of thymol poisoning, such as delirium, vertigo, and dark brown urine, must be regarded as indications that the use of the drug should be suspended for a time.

Eight days after a course of thymol the stools should again be examined microscopically; if ova are found to be still present the drug should be repeated. It is said that a certain proportion of the male and all the immature female ankylostomes resist its action.

After the expulsion of the parasites has been secured, the anæmia should be treated by iron, dieting, and on ordinary principles.

Prophylaxis.—In all countries in which ankylostomiasis is endemic great care should be taken to secure a pure water-supply. Where this is impracticable, all drinking-water should be boiled or filtered. Agriculturists, brick-makers, miners, and all those whose hands are apt to be soiled with earth or clay, must wash most carefully before eating. In villages and plantations those responsible for the health of the natives should prevent contamination of the water-supply and of the ground by the indiscriminate casting of night-soil about; and also insist on the systematic use of privy trenches, or other suitable contrivance, in which the fæces may be disinfected or effectually and permanently covered up.

Family—Trichotrachelida

So called from the long, thin neck at the end of which is placed a simple, punctiform mouth. The œsophagus in all the species constituting this family is also very long, and is further characterised by the cord of large and peculiar cells with which it is surrounded.

Trichocephalus hominis—(Synonyms: *Trichocephalus dispar*, Whip-worm).—This parasite, whose principal seat is the cæcum, measures in length, in the case of the male worm, 35 to 45 mm., in the case of the female worm 35 to 50 mm. It looks as if made up of two portions—(first) the long filiform neck which somewhat abruptly expands into (second) the thick and relatively short body; it reminds one in shape of a certain pattern of whip—hence its name in the vernacular.

In the male the posterior part, or body, is disposed in a spiral of one or two turns; it ends abruptly, the cloaca, from which the single spicule and its sheath usually protrude, being terminal. In the female the body is nearly straight and tapers gradually to the pointed end, the anus—a transverse slit—being subterminal. The vagina opens at the root of the neck. The cuticle in both sexes is transversely striated, and is further marked by a longitudinal band of minute papillæ extending from head to tail along the ventral surface. Uterus and testicle are single, and fill the thick posterior part of the worm. The long neck is occupied by the œsophagus only.

The ova, with which the uterus and capacious vagina are crowded, measure 0·05 to 0·056 mm. by 0·024 mm. They are oval, brown, thick-shelled, and are readily distinguished from all other intestinal ova by the clear pale bodies which mark both poles of the oval. At these points the shell is deficient, the holes so formed being plugged by a sort of tampon of a clear homogeneous material.

Like the ovum of *A. lumbricoides*, that of *T. hominis* contains no differentiated embryo on first leaving the parent worm; it has to pass a long time—many months, sometimes as many as eighteen months—in water before the embryo is developed and ready for direct transference to the human stomach. The ova are possessed of great resisting powers, and may be frozen or desiccated without permanent injury to their vitality. The embryo requires no intermediate host, but reaches the stomach in water or in food while still *in ovo;* here the shell is dissolved and the embryo liberated. In four or five weeks—as has been proved by direct experiment—the young parasites arrive at sexual maturity.

Although the usual situation of the trichocephalus is the cæcum, it is found at times in the other sections of the alimentary canal, even in the stomach. The latter is a rare event; but it is very often found at the lower end of the ileum, in the appendix vermiformis, and in the ascending colon. Usually it lies loose in the gut; occasionally, however, specimens are encountered which cannot be readily displaced, and which, according to Leuckart, have fixed themselves to the mucous membrane by transfixing a fold of it with their long necks as with a pin, the fine end emerging on the surface of the mucosa some distance from the spot to which the body seems to be attached. Other observers deny that these worms so fix themselves.

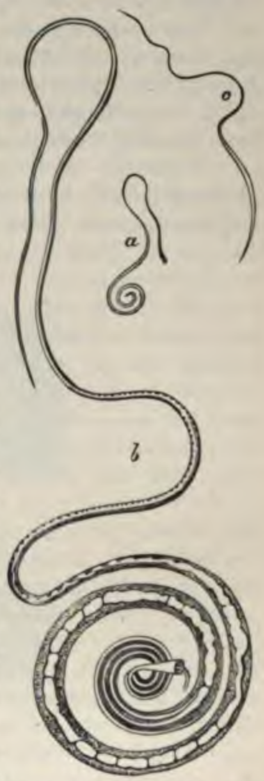

Fig. 44.—*Trichocephalus hominis.* *a*, male (nat. size); *b*, male (enlarged); *c*, female (nat. size). After Blanchard.

In *T. hominis* the sexes are about equal in numbers; if anything, the males are the more numerous. It is a rare thing to find more than a dozen or two specimens in a body, but every now and then cases of a high degree of infection are met with in which the cæcum contains hundreds and even thousands of these parasites.

In its geographical distribution the trichocephalus is cosmopolite. Speaking generally, it may be said to be more common in the inhabitants of warm than in those of cold climates. There are many local circumstances, particularly the character of the water-supply, which have an important influence in determining the proportion of inhabitants affected in any given place. In Paris, for example, Davaine believed that one-half the population were affected; in Dresden, of 1939 individuals in whom the trichocephalus was sought for it was found in only 2·5 per cent; in Erlangen, of 1755 individuals it was found in 11·11 per cent; in Kiel, of 611 individuals in 30·6 per cent. It is very common in the Malay Archipelago, as elsewhere in the tropics; thus in Sumatra Erni found it 24 times in 30 autopsies.

The trichocephalus, so far as known, has very little pathological significance. A few cases are recorded in which nervous symptoms were found in association with a high degree of trichocephalus infection. But there is no adequate ground for supposing, as some have asserted, that it is in any way responsible for such diseases as typhoid fever or beriberi.

Treatment.—Although these worms are often expelled accidentally by the male fern, santonin, or thymol administered for other kinds of intestinal worms, these drugs are by no means to be relied on as specific against trichocephalus. There is no good anthelmintic known for this parasite.

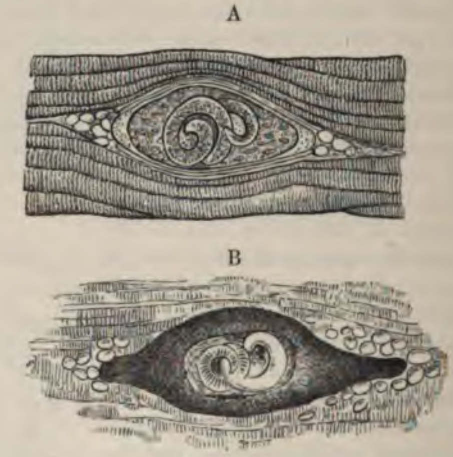

FIG. 45.—Trichina; capsule, with connective tissue covering. A, alive; B, capsule calcified.

Prophylaxis should consist in securing a pure water-supply, or in boiling or filtering drinking-water when it is not absolutely beyond suspicion.

Trichina spiralis.—Although the muscle, encysted, or larval form of *Trichina spiralis* (Fig. 45) had been previously seen by one or two observers, to Sir James Paget belongs the merit of being the first to recognise the true nature of these bodies. His discovery was confirmed by Owen, who, in 1835, gave the parasite the name by which it is still known. Since that time much attention has been paid to the subject, principally by German observers; so that at the present day the life-history of the parasite and the important pathological states to which it gives rise are fairly well understood.

If the voluntary muscles of a man or other animal affected with trichiniasis be examined with a lens, and the examination be made any time after the fifth or sixth week from the date of infection, an innumerable multitude of minute cysts, each including a tiny coiled-up worm, can be seen dotted about the tissue and lying between the fibres and slightly separating them. If a fragment of the affected muscles be excised, laid on a glass slip, teased out, lightly compressed beneath a cover-glass, and then examined with a magnifying power of some forty or sixty diameters, as the slide is slightly warmed, or a solution of potash added to it, the little worm is seen to move. It is therefore alive. This is the encysted or larval form of *Trichina spiralis.*

The cyst, in which the trichina lies surrounded by a clear albuminous fluid, is oval or, rather, lemon-shaped in form, having two more or less pronounced diverticula at the poles. Its long diameter, which corresponds in direction with the muscular fibres, may be set down on an average at 0·4 mm., and its short at 0·25 mm. The capsule of the cyst is chitinous in character and lamellated; it varies a good deal in thickness according to the part of the cyst examined and to its age, being always thickest at the poles and in the oldest cysts, and least dense and most transparent in young cysts and about the equator. Some cysts are more globular than others. Most of them contain only one trichina, but cysts containing two or more, even up to six or seven, are frequently encountered.

In cold and dead muscle the included trichinæ are quite passive, and lie rolled up dorsally in a close spiral of four or five turns. In warm and fresh muscle the spiral is more open, and more in contact with the cyst wall, over which the head end of the worm is seen slowly to move. The worm itself is cylindrical, tapered off anteriorly to relatively small dimensions, thicker posteriorly where it is abruptly rounded off. It measures from 0·8 mm. to 1 mm. in length. The mouth opens at the fine end, the anus at the thick end; an alimentary canal of the type characteristic of the trichotrachelidæ running between these two points. In addition to the straight alimentary canal the rudiment of the sexual organs can be made out as a thick tube occupying the greater part of the ventral portion of the posterior half of the body; development in this respect, though not complete in the encysted worm, is well advanced, the sexes being already distinguishable.

If a piece of raw flesh containing these encysted trichinæ be eaten by man or by certain of the lower animals, the cysts are dissolved by the gastric juices and the parasites liberated; they then quickly pass into the small intestine, where the sexual organs, already well advanced, rapidly complete their development. At the end of one to two days impregnation is effected.

At this stage the worms have grown slightly—the male to 1·2–1·6 mm., the female to 1·5–1·8 mm. Both sexes retain their cylindrico-conical shape, but the male is now seen to be provided at the posterior end with two appendages resembling the jaws of a pair of pincers. These organs form a sort of copulatory bursa, their function being to fix the female *in coitu.* The male has no spicule, but the cloaca can be evaginated, thus forming a sort of penis. Between the caudal appendages lies the cloaca, and behind the cloaca two small papillæ. In the female the single ovarian tube runs forward to terminate in the vulva on the ventral surface about the junction of the anterior with the second fifth of the body. In both sexes the oral end is very finely pointed, carrying at its tip the punctiform mouth.

When copulation takes place the female has not attained her full size; she is then but little larger than the male worm. Impregnation effected, however, the male worm dies and the female grows rapidly to two or three times (3–4 mm.) her original size. Growth takes place principally in the posterior part of the body, and is apparently a consequence of the rapid development of the ovarian contents. The trichina is ovo-viviparous. The upper part of the oviduct is filled with segmenting ova; lower down the embryo becomes apparent, enclosed in its vitelline membrane; lower still this membrane disappears and the embryo is free. The first of the young trichinæ are born about the sixth or seventh day from the date of infection. The parent worm continues to pour forth her young in a continuous but, after a time, diminishing stream during the following five or six weeks, when, after having given birth to a swarm of many thousands, she dies and is voided.

The young trichinæ, which are minute, lancet-shaped organisms with a thick, rounded anterior end gradually tapering to a fine tail, measure about 0·1 mm. by 0·006 mm. Soon after birth they penetrate and traverse the walls of the intestine, cross the peritoneal cavity, and, travelling along the connective tissue spaces, finally come to rest in voluntary muscle and in certain other tissues. During this journey, which, according to the distance travelled, may last a longer or shorter time up to ten days, the trichina increases slightly in size, and traces of an alimentary canal begin to appear. On arrival at its destination, which, according to some, is the inside of a muscular fibre, according to other and more recent views the connective tissue between the muscular fibres, it gives rise, by its movements and its presence, to a certain amount of irritation, leading to proliferation of the connective tissue cells in its immediate neighbourhood. In the exudation so produced, and probably from this exudation, the capsule of the cyst, already described, is moulded, the moulding process possibly being effected by the rotatory movements of the worm now passing into its larval and passive state. Some helminthologists believe that the cyst wall is formed, not in the way described, but very much as the cyst wall of the trematode larvæ is formed; namely, from a secretion proper to the animal itself.

Step by step with the progress of encystment the parasite gradually ceases to move; it then coils itself up and, increasing in size, assumes the larval characters already described. Eighteen days from the time of infection this process is complete; after that the young larva, on being transferred to the stomach of another animal, is capable of attaining sexual maturity.

In the encysted state the trichina retains its capacity for further development for many years—five, ten, even twenty years. Ultimately, however, the cyst undergoes fatty and calcareous changes, and the parasite it contains dies.

Such, briefly, is the life-history of *Trichina spiralis.* It is manifest that, cannibal countries excepted, man cannot possibly be the normal host of the parasite; nor, although the pig is the invariable medium of infection for man, can we regard even the pig, which in a state of nature has few opportunities of indulging its carnivorous propensities, as the proper host. It is believed that *Trichina spiralis* is normally and properly speaking a parasite of the rat; and that its occurrence in other animals is more or less of an accident depending on the artificial conditions of life imposed by civilisation. Rats are known to devour each other as well as the dead bodies of any other animals they may chance to come across; and it is believed that it is by this animal and in this way that, in the natural order of things, the species *Trichina spiralis* is kept in existence and transmitted. Systematic examination of the rats of different countries proves the extreme liability of this rodent to trichina infection, and tends to bear out this view. Thus an investigation in Germany showed that 8·3 per cent of the rats in certain places were trichinised. A similar inquiry

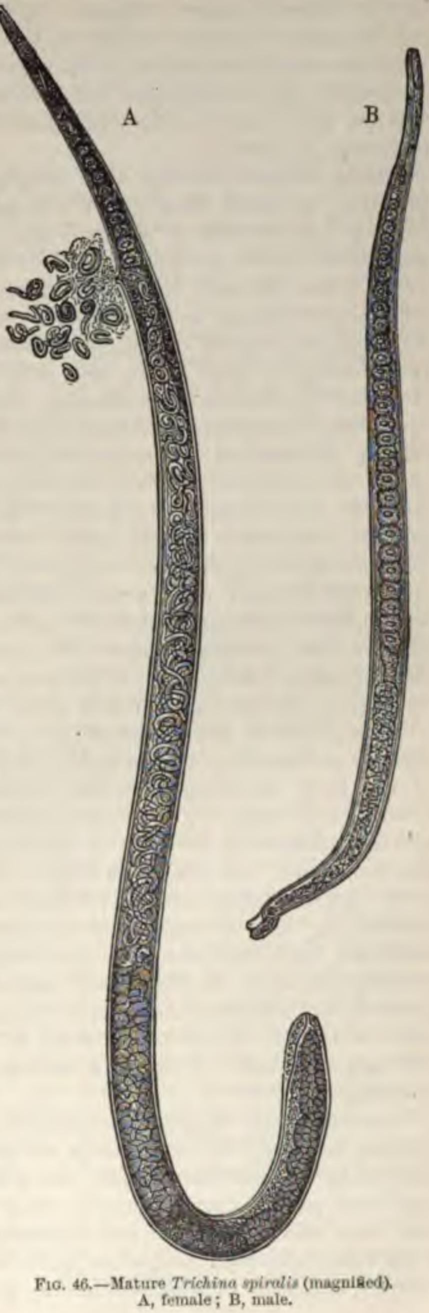

FIG. 46.—Mature *Trichina spiralis* (magnified).
A, female; B, male.

in the United States of America yielded still more remarkable results; for in some localities 10 per cent of the rats were affected, in other localities even 100 per cent. Impressed by these and similar facts some naturalists have suggested that *Trichina spiralis* was introduced into Europe from Asia by the gray rat, which first made its appearance in Germany in 1770.

It is further believed that the pig in the first instance is very often infected by eating dead and trichinised rats which had died in or been thrown into its sty, or which it may have come across and devoured in the course of its grubbings. The liability of the pig to infection, however, is further and very much increased by the thoughtless way in which, too often, it is fed on kitchen slops, on scraps of offal, and on the washings and refuse of slaughter-houses, which may very well contain—particularly in large killing and packing establishments such as those in America—fragments of trichinised swine's flesh. In this way the offal of a single trichinised carcase may infect an entire herd; and one can readily conceive of circumstances, particularly in those large establishments in which swine are bred and fattened as well as slaughtered, whereby this systematic feeding on offal must inevitably lead not only to general trichiniasis of the stock, but to an increasing and finally an extreme degree of this most dangerous form of parasitism.

Another point of practical importance is the circumstance, now thoroughly established, that the larval trichinæ encyst themselves, not only in the voluntary muscles, but also in the connective tissue of many other organs, notably in the panniculus adiposus and in the coats of the intestine. In this way it comes about that they are to be found in lard, in sausage skins, and in other food preparations, which might be looked upon as unimportant by-products of the pork factory. Of all the muscles of the body the diaphragm, and particularly its pillars, is most subject to trichiniasis; next to it the intercostal muscles; the muscles of the neck, and the muscles of the eye: in the larger muscles the parasites are most numerous near the tendinous ends. Now it so happens that these parts form just the scraps which in economically conducted establishments are worked up into sausages and similar preparations; hence the many accidents that have occurred from eating such things when imperfectly cooked. Next to those already enumerated the muscles of the upper part of the trunk are most liable to infection; then those of the lower part of the trunk: of the muscles of the limbs, those nearest the trunk are most affected. It may be mentioned that the heart rarely contains trichinæ.

Another point of great practical importance is the remarkable resisting powers displayed by the trichina as against decomposition, high and low temperatures, desiccation, and the action of the chemical substances employed in pickling. Trichinæ which had lain in putrid meat for over 100 days were still alive; and Fourment has shown that the trichinæ in pork which had been steeped in pickle were still alive at the end of fifteen months, and were capable of infecting and killing mice in a very few days.

Benecke also has shown that the trichinæ in hams and sausages which had been in pickle for twelve days and then smoked were alive nine months afterwards. Neither are they killed by temperatures as low as − 20° C. Leuckart exposed a ham during a whole night in winter, and also during three days when the temperature ranged from − 22° to − 25° C., and yet the trichinæ it contained survived.

Still more remarkable and important is the tolerance by this parasite of high temperatures. Perroncito asserts that on the stage of the microscope an exposure of a few minutes to a temperature of from 48° to 50° C. suffices to kill it. Other observers, however, maintain that in other and more ordinary circumstances the parasite will resist a temperature of 60°, 70°, or even of 80° C. If this be so, it is evident that the trichinæ in the centre of a large joint of pork will not be killed by cooking as ordinarily conducted, and that the trichinæ in chops or cutlets apparently well cooked may still be alive. It has been shown that after two hours' boiling the temperature at the centre of a large ham had only risen to 33° C.; after six hours to 65° C.; and that it was only after ten hours' hard boiling that 85° C. was reached. Therefore, to be really effective against the trichina, the cooking of pork and ham must be much more prolonged and thorough than is customary. Little wonder, therefore, that several epidemics of trichiniasis have been caused by swine's flesh cooked in the ordinary way. That of Posen, occurring in 1863, in which seven persons were attacked after eating food which had been cooked for an hour and a half, is an instance in point; the Workington epidemic in 1871, as narrated by Cobbold, is another instance. That this is the only epidemic recorded as occurring in Britain is in some measure attributable to the thorough way in which food is cooked in this country as compared with Germany; the same remark applies to France, Italy, and especially to China.

Geographical distribution.—As rats and pigs are now found in all lands, *Trichina spiralis* is one of the cosmopolitan parasites. It is more common, however, in some countries than in others, its degree of frequency being probably in great measure influenced by the habits of the human inhabitants in the matter of pig-keeping and pig-feeding. In Great Britain it is rare; it is rare also in France and in Italy. It is common in America, Holland, Denmark, Sweden, and Germany. Thus of 53,318 pieces of American pork or preparations of pork examined at Havre, France, 1087 pieces or 2·03 per cent were found to contain trichinæ; observations made in different parts of America variously state the proportion of trichinised pigs at from 5 to 8 per cent. In Germany, at Rostock, one pig in 336 was trichinised; in Brunswick one in every 5172; and in Prussia one in about every 2000. In India the trichina is said to occur frequently. In China (Amoy) I found the parasite twice in 219 carcases.

Trichiniasis or **Trichinosis.**—For many years subsequent to its discovery *Trichina spiralis* was looked upon as an innocuous parasite,—a curiosity, but in other respects of no interest to the pathologist. In

1860 a series of brilliant discoveries by Zenker, Virchow, Leuckart, and others placed the matter in a very different light, and conclusively proved that the trichina and trichinised pork were responsible for many peculiarly localised and very deadly epidemics, the nature of which had not hitherto been understood.

In the year referred to a young girl died in hospital at Dresden, it was supposed of typhoid fever. A marked feature in her case had been severe pains in the muscles. At the post-mortem examination no ulceration of Peyer's patches was discovered. When Zenker came to examine the muscles, which had been the seat of so much pain, he was astonished to find that they were stuffed with trichinæ; and when, in consequence of this discovery, he directed his attention to the contents of the alimentary canal, he had no difficulty in finding there numbers of adult parent worms. The girl had evidently died, not of typhoid fever as was supposed, but of trichiniasis. Pursuing the subject Zenker traced the girl's infection to certain preparations of pork; and he further ascertained from the butcher who had supplied the meat that others among his customers, and several members of his own family who had partaken of the pork which had poisoned the girl, had been ill also, and all very much in the same way. Indeed, so many of his customers had suffered that he stopped the sale of this particular parcel of pork. Fortunately some fragments of the carcase had been preserved, and in this Zenker found multitudes of living encysted trichinæ. Henceforth trichiniasis took its place among well-established diseases, and a powerful stimulus was given to Virchow and Leuckart to continue the attempts they were then making to work out the life-history of the parasite; this, as we have seen, they succeeded in doing.

From all parts of Germany and from other countries evidence of the truth of Zenker's conclusions, and of the high practical value of his discovery, rapidly accumulated. Since that time from North Germany alone we have the records of over a hundred epidemics of trichiniasis. From America and from other countries we have similar records. So that at the present day trichiniasis has come to be regarded as a very real danger to certain populations, and one against which many sanitary regulations have been devised.

Symptoms.—These, of course, will depend on many circumstances; upon the number of encysted trichinæ swallowed, upon individual idiosyncrasy, upon the number of times the infection may be repeated, and so forth.

Roughly speaking, and taking a case of average severity, the symptoms of trichiniasis are divisible into three stages—each stage corresponding to a phase in the evolution of the parasite. There are—(first) the stage of intestinal irritation, commencing a few hours after the ingestion of the diseased meat, and corresponding to the growth, development, and sexual activity of the parent trichinæ, and to the penetration of the alimentary canal by their brood of young; (second) the stage of myositis, characterised by severe muscular pains and irritative fever, and produced by the injury done to the muscles by the migrating trichina embryos; and (third) the stage of subsidence, corresponding to the encystment of the larval trichinæ and gradual subsidence of the myositis.

In some cases these stages are well defined, particularly in severe cases. In others, again, particularly in cases of mild, or of mild and sustained infection, they are not well defined—vague rheumatoid pains being, perhaps, the only evidence of trichiniasis.

In an attack of trichiniasis of moderate severity the symptoms commence within a few hours, or, at most, a day of the ingestion of the trichinised meat. There is early evidence of more or less violent intestinal irritation—vomiting, diarrhœa, foul tongue and breath, and colicky pains, accompanied perhaps with cramps and cold extremities. So severe may these symptoms be that many times they have been mistaken for cholera. A large dose of uncooked trichinised meat is more likely to be followed by such symptoms than a smaller dose of partially cooked meat in which, it may be assumed, many of the trichinæ have been destroyed. The intensity of the intestinal irritation is, however, no guide to the danger of the case; for the very severity of the vomiting and purging is the means of expelling many of the parent trichinæ before their young are born and have penetrated the intestinal walls. Cases, therefore, which at the outset are attended with little or no diarrhœa or vomiting may be quite as dangerous in the long run as those with violent choleraic symptoms.

About the ninth or tenth day from infection, diarrhœa perhaps still persisting, the characteristic pains in the muscles set in, and gradually increase in severity. The muscles become swollen, hard like a piece of india-rubber, and very tender to the touch and on being put into action. Fever, too, is lit up by the myositis, and may run high—even up to 106° F.; usually, however, it is about 102° or 103°, with slight morning remissions. Movement causes pain, and the functions of many important muscles are seriously interfered with. Thus respiration may be affected by implication of the diaphragm and intercostals; mastication, speech, and deglutition by implication of masseters, tongue, pharyngeal and other muscles; phonation, by implication of the laryngeal muscles; expression, by implication of the facial and orbital muscles, and the pain of moving them. Standing, locomotion, movement of the hands and arms, are all very painful—sometimes impossible. The flexor muscles are especially affected. At this stage the patient lies in bed with his limbs maintained in a state of semiflexion, or in such position as entails a minimum of pain—just as in severe rheumatism.

In most cases about the eighth day the face, particularly about the eyelids, becomes puffy and œdematous; sometimes there is chemosis. This disappears in a few days. Later, however, about the fourth or fifth week, a much more extensive œdema occurs in 90 per cent of serious cases. It affects the limbs, often the trunk, neck, and face—usually sparing the genitals. It may come and go. This œdema is sometimes very great, more extensive even than that of acute nephritis.

Profuse perspirations, often accompanied by miliary eruption, are a usual symptom; beginning with the incidence of the myositis they may not cease to recur till convalescence has commenced. Pruritus may be troublesome in the earlier stages; later the skin may be covered with acne, pustules, or boils.

Wasting is very marked in severe cases; in fact all the symptoms of the typhoid condition may be presented. The tongue becomes dry, the pulse frequent; prostration may be great, and stupor marked. Not infrequently there is delirium, and nearly always in the adult there is insomnia—doubtless dependent on the pain in the muscles. Children are, on the contrary, always somnolent.

In many cases signs of bronchitis, of hypostatic congestion of the lungs, or of pneumonia set in. Much fluid accumulates in the air-passages, owing to debility and to the inability of the inflamed muscles of expiration to produce effective cough.

So the case goes on till about the fifth or sixth week, when convalescence may be looked for. The myositis gradually subsides, and in the course of a few weeks the patient is well again. Sometimes convalescence sets in earlier; on the other hand, the case may drag on for two or three months.

Death has occurred in rare instances in the first stage of the disease, from the collapse produced by choleraic purging. Generally the fatal event does not take place till the height of the myositis in the fourth or fifth week. It is usually the immediate result of asphyxia brought about by a high degree of myositis in the diaphragm and intercostal muscles; bronchitis and pneumonia, of course, add very much to the danger. Death may occur at a later stage from some complication, such as bedsore, pneumonia, marasmus, or general asthenia. Intestinal hæmorrhage and diarrhœa are also occasional causes of death.

The *mortality* from trichiniasis varies in different epidemics, and evidently depends on the dose of living trichinæ ingested; being greater, *cæteris paribus*, where the trichinised food is raw, or only lightly cooked, than where it has been thoroughly heated. Children nearly always recover. In Saxony, from 1860 to 1875, the aggregate mortality in 39 epidemics, affecting 1267 individuals, was 19, or about 1½ per cent. In an epidemic at Hedersleben, affecting 337 individuals, there were 101 deaths—nearly one-third.

Diagnosis.—Trichiniasis is readily recognised during an epidemic of the disease when suspicion has been aroused by the simultaneous occurrence of a number of cases in a particular place, and in an associated group of individuals; but in isolated cases diagnosis is by no means an easy affair. It is very apt to be mistaken for typhoid. The distinguishing points are principally the absence in trichiniasis of the initial headache, of the epistaxis, catarrh, and deafness, and, later, of the eruption and enlargement of the spleen characteristic of typhoid; and by the presence of muscular swelling and tenderness, and of œdema of the face and limbs. This œdema may suggest nephritis, but it is not associated with albuminuria as in this disease it would be. From rheumatism it may be distinguished by the situation of the pain in the muscles, and by the associated disturbance of the intestinal canal. Trichiniasis has frequently been mistaken for cholera, and, indeed, at first they may be hard to distinguish. It is said that in trichiniasis, during the first few days of the disease, there is a peculiar feeling of heaviness of the limbs, accompanied by a sensation of tension and pain, especially in the flexor muscles, causing the legs to be dragged in walking; this symptom is said to be long antecedent to the myositis of the second stage, and is valuable as a distinction from cholera. In all cases of doubt, however, particularly in presence of an epidemic, the microscope should be used to search the stools for adult trichinæ, and any suspected food for larval trichinæ. If necessary a small piece of muscle, best from the lower end of the biceps, may be excised with the knife; the harpoon designed by Middeldorpff for this purpose produces an unsurgical wound, and removes only a very small piece of muscle.

The symptoms of trichiniasis bear in many respects a very close resemblance to certain forms of acute multiple peripheral neuritis, especially to beriberi—a circumstance overlooked by systematic writers, but one, especially as regards beriberi, of practical importance to the physician practising in warm climates. Both diseases occur in localised epidemics, both may be associated with œdema, both are characterised by pain and tenderness in the muscles, and both may kill by asphyxia arising from impaired power in the muscles of respiration. The principal diagnostic marks are, in trichiniasis, the severe gastro-intestinal irritation and persistent fever; in beriberi, the early pretibial œdema, the patchy anæsthesia, the absent knee-jerks, the reaction of degeneration in the muscles, the cardiac bruits, the clean tongue, and good appetite. Trichiniasis presents the symptoms of a myositis, beriberi of a neuritis.

Treatment.—It is impossible to kill the embryo trichinæ after they have penetrated the intestinal walls and gained the tissues. Many drugs have been recommended with this object; they are manifestly useless, and need not be discussed. But it is possible to rid the patient of many, if not of all of the parent trichinæ in the alimentary canal; and, as it has been shown that these continue to produce embryos during several weeks, it is the duty of the physician to endeavour to get rid of as many of them as possible. His efforts in this direction should at all events be continued during the first three or four weeks of the disease. If the patient be seen soon after trichinised food has been swallowed a quick-acting emetic should be administered at once, and its action followed up by a smart purge. Calomel up to twenty grains is said to be the most effective cathartic, the dose being repeated several times; it is credited with the power of bringing away large numbers of trichinæ. It would appear that the ordinary anthelmintics are powerless against this worm. Glycerine in large doses has been recommended; it is supposed to kill the parasites by dehydrating them. It seems to me that thymol, given in full doses as for ankylostomiasis, is likely to prove as effective against the one worm as it is known to be against the other; this drug deserves an extended trial in the early stages of trichiniasis.

During the progress of the disease general treatment must be conducted on the same principles as for the continued fevers. Attention must be directed to maintaining the strength and the state of nutrition, special symptoms being treated as they arise.

Prophylaxis.—In Germany, where it is the custom of many people to consume uncooked preparations of swine's flesh, the systematic examination of all carcases with the microscope is conducted by a regular service of official experts. A small piece of muscle is snipped from the diaphragm and three or four other muscles, placed on a slide, teased out with needles in one per cent solution of salt, compressed below a cover-glass, and examined with a magnifying power of about sixty diameters. Any trichinæ the preparation may contain are easily recognised. If they are alive, a slight warming of the stage causes them to move: if they are dead, they colour at once on adding aniline blue solution to the preparation; living trichinæ do not take the stain.

Similar precautions are or were taken in other countries against imported American pork. In France the importation is interdicted. In England such precautions are not taken, being rendered superfluous by the comparative freedom of our native swine from trichiniasis, and the habit of thoroughly cooking pork, hams, sausages, and all similar preparations before bringing them on the table.

Thorough cooking is the best preventive of trichiniasis; and it must not be overlooked that such things as sausage skins, lard, etc., may contain trichinæ. A safe course is to boil a joint or ham thirty-five minutes for every kilogramme it weighs.

Attention should be paid to the prevention of trichiniasis in swine. Their sties should be kept clean and free from rats. Above all they ought never to be fed on uncooked offal. This last precaution must be particularly attended to in large feeding and killing establishments.

Family—Filarida

The *filaridæ* are long filiform worms with a lipped, a papillated, or a simple mouth. The tail of the male is strongly incurvated, and is furnished with four pairs of pre-anal papillæ, and sometimes an additional single unpaired pre-anal papilla, besides an uncertain number of post-anal papillæ. The male has either a single spiculum or two unequal spicula. In the female the uterus is double. The family includes many genera, only one of which—*Filaria*—is represented among the parasites of man.

Filaria inermis is properly a parasite of the ass and horse; it is about 16 cm. long by 0·475 mm. broad, white, and slightly flattened.

The mouth is terminal and simple; the vulva is placed close behind the mouth. The species is ovo-viviparous, the more mature embryos being free at the lower end of the uterus. These are rounded anteriorly, gradually tapering to a pointed tail posteriorly, and measure 0·35 by 0·005 mm. Neither the male worm nor the life-history of the parasite is known. *F. inermis* has been found in man, in an immature state, only three times, namely, once in the eye, once encysted in the gastro-splenic omentum, and once encysted in the ocular conjunctiva.

Filaria oculi humani.—Under this name are included probably several species of minute filariæ which, from time to time, have been found either in the crystalline lens, in the vitreous, or in the aqueous humours. Similar parasites are found in the lower animals; it is probable that those which have been found in man are normally parasitic in beasts. Their zoological characters and pathological effects are equally unknown.

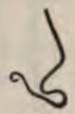

Fig. 47.—*Filaria loa* (nat. size). Dr. Logan.

Filaria restiformis, Filaria hominis oris, Filaria labialis, Filaria lymphatica, Filaria volvulus.—Each of these has been found once or twice in man. As they appear to be properly parasitic of the lower animals, and to have little practical interest as regards man, the reader is referred to systematic works on helminthology for further information.

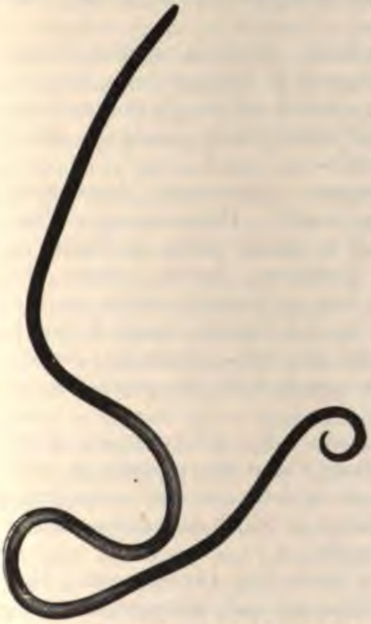

Fig. 48.—*Filaria loa* (magnified). From a photograph by Mr. Andrew Pringle.

Filaria loa is indigenous and confined to the West Coast of Africa, where, in many districts, it is not uncommon. It lives in the subcutaneous areolar tissue, wandering about the body, and causing, when it approaches the skin, a certain amount of localised itching and irritation. It occasionally appears in the eyelids or under the conjunctiva, and there gives rise to much pain and congestion. *F. loa* is usually from 30 to 40 mm. long, and about as thick as a fine fiddle-string. Its anatomy and life-history are very imperfectly known. It is ovo-viviparous in the sense that when the embryo leaves the parent it is still enclosed in the egg-shell, which now forms a sheath as in *Filaria nocturna* and *Filaria diurna*; considering this circumstance, its location, the characters of its embryos, and its peculiar geographical distribution, it may be that *F. loa* is the mature parental form of *F. diurna* (p. 1066). Recently I had an opportunity of examining three specimens of this parasite. Two of them had been removed by Dr. Argyll Robertson from an English lady who had resided for some time in Old Calabar; one of them—the first removed—was a male. After an interval of several months the second parasite appeared and in the same eye; it proved to be a female. Dr. Logan of Liverpool also removed some time ago a male *F. loa* from the eyelid of an Englishman long resident in Western Africa. From these three specimens many of the characters of this parasite could be made out. The male (Figs. 47, 48) measures 25 mm. in length by 0·3 mm. in breadth; he has a simple mouth, an incurvated tail, carrying two rather short unequal spicules, and at least five pairs of papillæ, four of the pairs being very large. The chitinous integument is sprinkled over with numerous hemispherical bosses. The female worm is considerably larger; it is probably to her that Leuckart's measurements given above refer. Her integument is also besprinkled with chitinous bosses.

Treatment.—Excision. It is the custom among certain tribes of negroes to drive it from the eye by placing a few grains of salt in the conjunctival sac; sometimes they remove it by means of a sharp thorn used as a needle.

Filaria medinensis—(Synonyms: *Dracunculus medinensis*, Guinea-worm, Dragonneau).—This parasite is endemic in many parts of India, in Persia, Bokhara, Turkestan, Arabia, along the coasts of the Red Sea, in Tropical Africa, and in one or two spots in the tropical parts of South America. In some of these places at certain seasons of the year nearly half the population is affected.

Although as a rule only one worm is present at a time, in countries where the parasite is very prevalent two, three, or four are not uncommon; and cases are on record in which as many as thirty coexisted in one person.

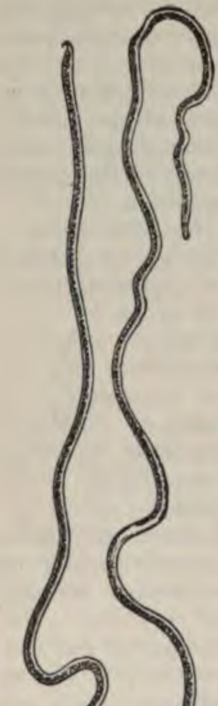

FIG. 49.—*Filaria medinensis* (nat. size). Leuckart.

Only the female worm (Fig. 49) is known. Her habitat is the subcutaneous and intermuscular connective tissue. Here, unconsciously to the host, she attains a great length. Some specimens measure as much as six feet, others again not more than one foot; three feet may be stated as an average length. The breadth is about one-tenth of an inch. The head end of the worm is slightly tapered down, and then abruptly truncated. The mouth is terminal, and surrounded by two large and six smaller papillæ. The body is white, faintly transversely striated, uniformly cylindrical, firm, very extensile, and having a breaking strain of about eleven ounces. The tail terminates abruptly—usually in a small, sharply-bent hook. The alimentary canal, thrust to one side and compressed by the gravid uterus, is a fine tube which runs backwards from the mouth to near the tail, where it terminates, without opening externally, by merging in the musculo-cutaneous body-wall. There is no vagina; this appears to have been obliterated at an earlier stage by the inordinately developed uterus. The latter organ runs from head to tail as one continuous and, relatively, enormous tube packed with millions of free embryos.

I have recently pointed out elsewhere the process by which the embryo dracunculi quit the body of the vaginaless parent worm and that of their human host; it is an interesting one, and has a very practical bearing on treatment. When the parent dracunculus approaches maturity, she begins to move slowly through the tissues, head first, and, in 90 per cent of cases, in a downward direction until her head arrives at foot, ankle, or leg. The head then drills a small hole in the derma, sparing the epidermis. Over this hole a bulla forms, probably induced by the irritating properties of some secretion or discharge from the worm. In the course of a few days the bulla ruptures, disclosing a small superficial ulcer with the aforementioned minute hole in its centre. Sometimes, on rupture of the bulla, though this is by no means usual, the head of the worm is seen protruding from this little hole. If now, whether the head protrude or not, a little cold water be poured on the limb in the vicinity of the dracuncular ulcer, a minute quantity of a whitish fluid is presently seen to well up from the central hole; or a small tube, at first pellucid, then white, is seen to be slowly extruded from this hole to the extent of about half an inch or even more. Suddenly this little tube ruptures, its contents being spilt over the ulcer. The whitish fluid alluded to is part of the uterine contents, and the little tube is part of the uterus itself, which the worm, stimulated by the water poured on the limb, forces as a prolapsus through her mouth. That this is what takes place is proved by a microscopic examination of the fluid referred to, which consists of a mass of seething, wriggling dracunculus embryos. This discharge, with or without visible prolapsus of the uterus, is repeated at short intervals. In the course of about a fortnight the worm has extruded, and emptied her entire uterus. She is now ready to quit her host, and often she will do so spontaneously. Generally she can be readily removed by gentle and intermittent traction renewed at intervals during a day or two.

The reason why instinct leads the dracunculus to descend to the foot or ankle before beginning to empty her uterus is obvious. These are just the parts of the body which, in a warm climate and in natural conditions of life, are most likely to be brought in contact with water. The reason why the extrusion of embryos is provoked by contact of the limb with water is equally obvious, for the next step in the development of the embryo is made in this element. It is true that the dracunculus sometimes reaches the surface at other points of the body, but such an event is comparatively rare and manifestly abnormal.

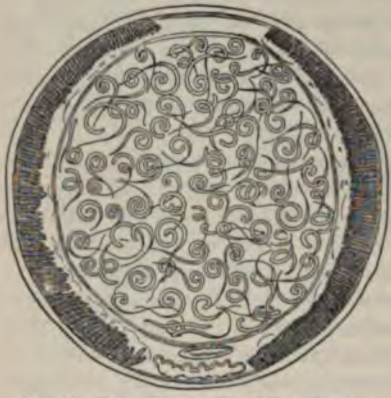
FIG. 50.—Transverse section of *F. medinensis*. Leuckart.

The embryo dracunculus (Fig. 51) (0·6 by 0·0175 mm.) is a long, transversely striated animalcule, provided with a slender tail occupying about two-fifths of the entire length. A rudimentary alimentary canal and two curious little sacs (Fig. 52) placed *vis-à-vis* at the base of the tail are readily made out. The body of the embryo is not cylindrical; it is distinctly flattened. The little animal swims about in the water very actively, and can be kept alive, especially in muddy water, for at least a fortnight. It can be resuscitated even after desiccation.

Its next step in development, as pointed out by Fedschenko, is made in a fresh-water cyclops, whose body cavity it enters by penetrating the joints between the ventral plates. In the cyclops the young filaria undergoes a metamorphosis which is completed in about five weeks. In this condition it is believed that the filaria is transferred to the human stomach in drinking-water. It is conjectured that the cyclops is therein digested; and the parasite, being thus set free, penetrates the alimentary canal. Nothing is known as to when or where impregnation occurs. It is believed that the parent worm takes about a year to reach maturity.

I have twice repeated Fedschenko's experiments with embryo guinea-worms procured, in the way I described, from Lascar patients in the Seamen's Hospital, Albert Docks, using cyclops from ponds in the neighbourhood of London. Placing the embryos and the cyclops together in a watch-glass in the evening, on the following morning I found that many of the young guinea-worms had transferred themselves to the body cavity of the cyclops, where they could be readily seen, in some instances in prodigious numbers, wriggling about quite actively. In my experiments metamorphosis occupied a much longer time than in Fedschenko's; for after seven weeks the first ecdysis and shedding of the tail had only been completed in some of the worms, others being still provided with tails and transversely striated integument. Probably this delay was owing to the lower temperature of our English climate; but from what I have seen I have not the slightest doubt that Fedschenko's statements about the rôle of cyclops in the life-history of the guinea-worm are

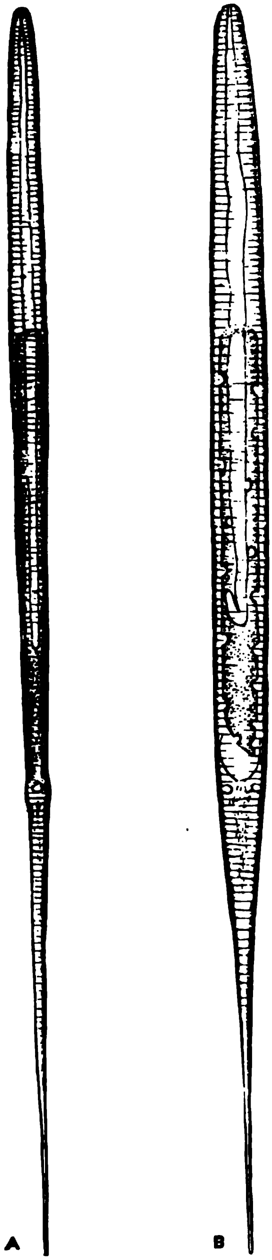

Fig. 51.—*F. medinensis* (× 250). A, side view; B, front view.

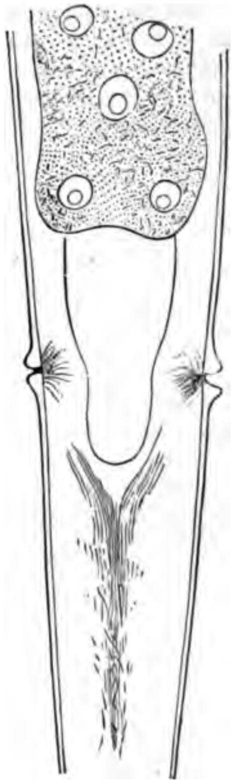

Fig. 52.—*F. medinensis*, showing lateral caudal sacs partially everted (highly magnified).

substantially correct. The embryo guinea-worm will not enter the body of daphnia.

Duke says that the appearance of a guinea-worm is usually preceded by a transient urticarial eruption often accompanied by vomiting. Beyond this, the occasional feeling as of a cord below the skin, and the bulla as before described, the worm, if not interfered with, gives rise at first to no symptoms. Should unintelligent attempts at premature extraction lead to rupture of the parasite, the consequent extravasation of millions of embryos into the tissues is almost sure to give rise to violent constitutional disturbance—to abscess, sloughing, and similar local troubles.

Treatment.—When she first shows herself the worm should be left alone and carefully protected by frequently renewed water-dressings. The parts ought to be douched several times a day with cold water to encourage parturition and uterine extrusion. When she is quite empty and begins spontaneously to emerge, her exit may be facilitated and accidental rupture prevented by rolling the body, as it emerges, on a piece of wood such as a match. Injudicious attempts to wind the worm out before she has emptied herself are to be deprecated, as they are nearly sure to end disastrously. If the entire worm can be made out distinctly coiled up just under the skin, she may be removed through a small incision, a loop being hooked up with a finger, whilst the surrounding tissues are carefully kneaded. Lately, injections of solution of bichloride of mercury (1 in 1000) into the track of the worm, injecting it as soon as the parasite begins to irritate the skin, have been advocated. One injection suffices. The worm is killed and is said to be absorbed like a piece of aseptic catgut. Recent observations seem to establish the value of this treatment.

Occasionally the guinea-worm fails to penetrate the skin or dies at an earlier stage of development. The worm in this case becomes cretified, and sometimes may be felt as a hard convoluted cord under the skin of the leg. Such cretified worms do no harm and ought not to be interfered with.

Filaria sanguinis hominis.—This term is applied to the free hæmatozoal embryos of various species of filarial parasites whose parental forms lie in the tissues, lymphatics, or blood-vessels; and whose young circulate in the blood of man. From the date (1872) of Lewis's discovery—that the blood of man occasionally contains these embryo parasites—up to the last few years, it was supposed that there was only one such species of blood-worm. Recently, however, I have shown that the subject is very much more complicated, and that there are at least four if not five such hæmatozoal embryos, each belonging to a separate and distinct species, and each probably having its own special pathological relations.

It is very probable that many more species of such hæmatozoa will be discovered hereafter. It would seem that the human blood, as well as the blood of many of the lower animals, especially of birds, is a fitting nursery for the young of an extensive fauna.

It is of the utmost importance, therefore, if we would avoid hopeless confusion and advance this new departure in pathology, that the greatest care be taken to identify the different species—diagnosing one from the other as carefully as we would small-pox from measles, pathogenetic from saprophytic micro-organisms, venomous from harmless snakes. It is not sufficient to chronicle in the record of a case that "filariæ were found in the blood"; we must specify the species, and, if it be a new one, describe accurately its appearance and habits.

The *Filariæ sanguinis* are long, slender, transparent, gracefully-formed, snake-like organisms which, when seen under the microscopic in newly-drawn blood, exhibit a remarkable activity in coiling and uncoiling themselves, in wriggling and lashing about in incessant and rapid movement among the corpuscles. They remain alive—their movements gradually slowing down, however—for days on the slide, provided the blood be kept from drying up and at an ordinary temperature. Unless possessed of considerable experience it is difficult for the observer to arrive at a diagnosis of any particular specimen of filaria when it is first mounted on the slide; but, as movement slows down, diagnosis of species is by no means difficult if the following points be attended to:—

1. The presence or absence of periodicity in the appearance and disappearance of the embryos in the blood; and, if periodicity be detected, its mode. Thus one species of filaria (*F. diurna*) appears during the day, disappearing during the night; another species (*F. nocturna*, Lewis's filaria) appears during the night, disappearing during the day; whilst two species (*F. perstans* and *F. Demarquaii*) are constantly present both by day and by night.

2. The presence or absence of a sheath enclosing the worm. Thus *F. diurna*, *F. nocturna*, and *F. Demarquaii* are enclosed in long, trailing sheaths, whereas *F. perstans* is, so to speak, naked.

3. The shape and characters of the head and tail ends of the embryo worm. Is the former provided with an armature, and if so, what are its characters and appearance? Is the tail acutely pointed or abruptly truncated, and what is the length of the taper running up to the tail?

4. Accurate measurements of length, breadth, and other features.

5. Character of movements: lashing and stationary as in *F. diurna* and *F. nocturna*, lashing and locomotor as in *F. perstans*.

6. Associated pathological conditions if such be present.

7. Country in which the parasite was acquired.

8. Zoological characters and exact seat of any parent worm which may be found.

If attention be given to these points a correct diagnosis can be arrived at in most instances.

Technique.—To ascertain the presence or absence of filariæ in the blood of man or animal the most rapid and, at the same time, most trustworthy method I have employed is the following, which has the additional advantages of not entailing microscopic examination until such time as may suit the convenience of the observer ; moreover, dealing as it does with a comparatively large quantity of blood, it is sure to reveal the parasites if any be present and free in the circulation. The blood is procured in the ordinary way, from a finger in man, or, in the case of the lower animals, from any part not covered with hair. When a large drop has welled up from prick or incision the entire amount is transferred to a glass slip by dabbing the centre of this on the blood. The blood is then spread out on the slip with a needle in a fairly uniform film, extending over an area of about one inch by one inch and a half. The slip is then laid on its uncharged surface till dry. The blood may be stained as soon as it is dry ; or the slip may be labelled and packed away till a more convenient time. The blood is best stained by immersing the slide for about an hour in a very weak watery solution of fuchsine, one or two drops of the saturated alcoholic solution to the ounce of water ; or, more quickly, by a 2 per cent solution of methylene blue. If it be found too deeply stained, it may be decolorised by washing for a few seconds in a weak solution of acetic acid, three or four drops to the ounce of water. It may then be examined wet or dry, with or without a cover-glass. A magnifying power of sixty to eighty diameters suffices to show the filariæ, which, with certain white blood corpuscles—in the case of fuchsine preparations—are the only stained objects in the field. Rapidity and thoroughness are secured by using a mechanical stage.

To study the movements and anatomy of the filariæ, slides of fresh blood must be used. Ordinary wet preparations are made, care being taken that they are not too thick ; the film should be no deeper than one row of corpuscles. If the examination is to be prolonged, or if it is to be renewed at intervals during several days, the slides had better be sealed with vaseline. Search should be made for the filariæ with the low power mentioned ; when they are found they can be centred and examined with higher powers. To see the sheath a magnifying power of 400 diameters suffices ; to make out the structure of the head and the V-spot a good condenser and an immersion lens are necessary, a moribund filaria in a field free from corpuscles being selected for study.

Filaria sanguinis hominis diurna.—Only the free embryonic form of this parasite is known. The writer found it three, possibly four times in the blood of negroes from the West Coast of Africa, from Old Calabar, from Dahomey, and, possibly, from Banza Manteka on the Congo.

Excepting that *F. diurna* appears in the blood during the day it closely resembles *F. nocturna*, being sheathed, sharp-tailed, possessing a central granular aggregation, a V-spot, and having similar dimensions, oral and general movements (see *F. nocturna*, p. 1068).

The diurnal periodicity of *F. diurna* has been thoroughly made out. As regards the parasite this is an important physiological fact, and is sufficient to establish the specific independence of this filaria from *F. nocturna*, seeing that it implies a different intermediate host, a different life-history and therefore a different parental form. Ordinarily *F. diurna* begins to appear in the peripheral circulation about 8 A.M., increases in numbers till about 12 or 1 P.M., decreases in numbers as evening approaches, and disappears for the night about 9 P.M. This periodicity I have observed maintained during many weeks.

Basing the conjecture on the fact, which after all might have been but a coincidence, that one of my *F. diurna* patients had previously suffered from *F. loa* under the conjunctiva of one eye, I have suggested that *F. loa* may be the parental form of *F. diurna.* Their identical geographical distribution—both, so far as known, being confined to the West Coast of Africa—favours such a supposition.

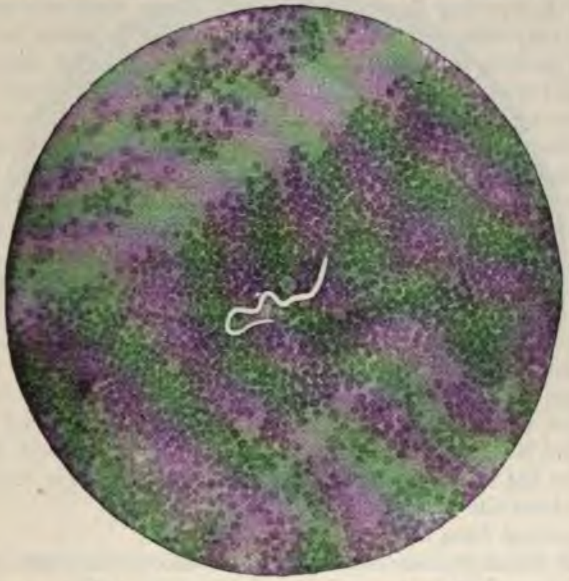

FIG. 53.—*F. perstans* (×160). From a micro-photograph by Mr. Andrew Pringle.

The intermediate host is unknown. Possibly it is a blood-sucking dipterous insect—*Chrysops dimidiatus*, the "mangrove fly"—which abounds and is very troublesome and voracious on some of the West African rivers.

So far as known, *F. diurna* is not responsible for any pathological condition.

Filaria sanguinis hominis perstans (Fig. 53).—This blood-worm is considerably thinner and shorter than *F. diurna* and *F. nocturna.* It is further distinguished from them by not possessing a sheath, by its truncated tail, by the absence of a central granular aggregation, by the characters of its oral armature, by its movements, and by the absence of periodicity.

Its average dimensions may be set down at ·23 mm. by ·0045 mm.; but as it has the habit of extending and attenuating, and of shortening and thickening itself as it travels about in the blood, an approximate and average measurement only can be given. As already mentioned it has no sheath. The thickest part of the body is about one-third of the distance back from the head; from this point it gradually slopes off to the abruptly truncated tail. The body is homogeneous throughout, no central granular aggregation and no V-spot or other distinguishing feature being visible. The head end is armed with a minute, exceedingly delicate, filiform spine set on what looks like a papilla. This spine and papilla are constantly and rapidly protruded and retracted. In addition to very active wriggling movements *F. perstans* travels about, often very rapidly, among the corpuscles, the attenuation and extension of its body facilitating its peregrinations. At no time very numerous—sometimes only three or four on a slide, rarely as many as twenty or thirty—*F. perstans* can be found as readily by day as by night. It may be associated with *F. diurna* or with *F. nocturna*, or with both.

Considering its remarkable locomotor habits, its cephalic armature, and the absence of the sheath which in other blood-worms acts as a muzzle, I believe that *F. perstans* leaves the blood-vessel by its own efforts, and has a somewhat different life-history from the sheathed and non-locomotive filariæ. What this life-history may be is at present a matter of conjecture.

So far as known, *F. perstans* is strictly confined to the West Coast of Africa and adjoining "hinterland." There, in some districts, quite two-thirds of the inhabitants are affected by it; in other districts it is not so prevalent, whilst in yet others and neighbouring districts it appears to be absent. I found it in the blood of negroes from the Congo, from Old Calabar, and from other places on the West Coast; but I entirely failed to find it in the blood of fifty Dahomeyans, nor could I find it in the blood of the many Africans I have examined from the East Coast, or in negroes from the West Indies.

The parental form of *F. perstans* is unknown.

Certain circumstances common to this blood-worm and the peculiar African disease called sleeping sickness or negro lethargy point to a probable relationship between the two. Thus both are indigenous and strictly confined to the West Coast of Africa and adjoining countries; both affect certain districts in this area in an apparently capricious way; both can be exported as it were, remain dormant for many years, and then declare themselves; neither is directly communicable; both affect all ages, both sexes, and any occupation; neither is hereditary, and neither is curable. These are remarkable and suggestive coincidences, the significance of which is further accentuated by the fact that *F. perstans* has frequently been found in the blood in sleeping sickness. [*Vide* art. on "Sleeping Sickness," p. 484.]

Filaria sanguinis hominis nocturna (Fig. 54) was first discovered by Demarquay, in 1863, in the fluid from a chylous dropsy of the tunica vaginalis; later, in 1864, it was found in chylous urine by Wucherer, and, as already mentioned, in the blood by Lewis in 1872. Since that time it has been found in the blood and in morbid discharges in many countries, from England on one side of the equator to Australia on the other. Its geographical range is therefore an extensive one. Practically, however, it may be said to be a prominent pathological factor in tropical and subtropical countries only, and in these more especially in particular districts. In some places (for example, Amoy, Bahia) it is to be found in quite 10 per cent of the population; in other places (for example, Cochin) in as many as 30 per cent, or even 50 per cent (Samoa). Speaking generally, its rarity or its frequency seems to depend on the presence of particular species of mosquitoes, on the character of the water-supply, and on the habits of the natives with regard to the use and storage of water. It is probable that the degree of prevalence of elephantiasis is an indication of the degree of prevalence of *Filaria nocturna* among the natives of a country.

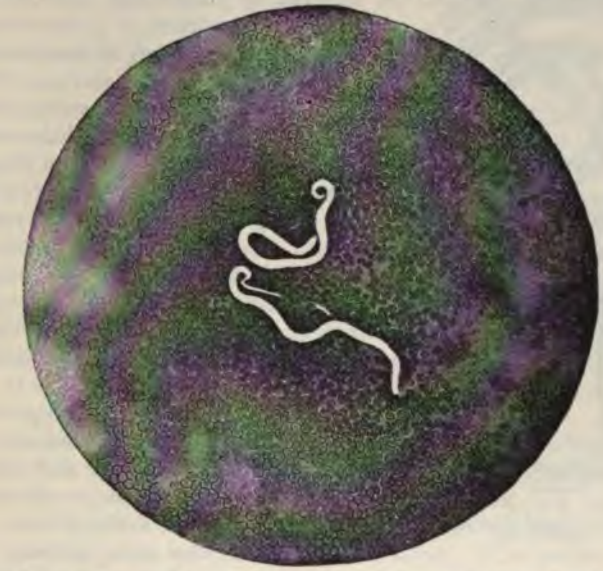

Fig. 54.—*Filaria nocturna* (×160). From a micro-photograph by Mr. Andrew Pringle.

The general features of the embryo-hæmatozoal stage of this parasite have already been sufficiently described. Its special characteristics are—its dimensions—a little over or under 0·3 mm. by 0·0075 mm.; its sharp pointed tail having a taper of about one-fifth of the entire length of the animal; an ill-defined granular aggregation, usually visible for a short distance around the axial line of its body about the junction of the middle and posterior third, which by particular methods of staining can be shown to be a hollow viscus; a minute, luminous V-shaped spot (probably connected with rudimentary water vascular system), with its apex opening on the surface of the body, and placed a short distance behind the cephalic extremity; a similar but much smaller spot near the end of the tail; and the cephalic armature. The latter consists of a retractile and pretractile six-lipped prepuce, covering and uncovering a thick, hemispherical proboscis, which is further provided with a minute, filiform, protrusible, apical spine.

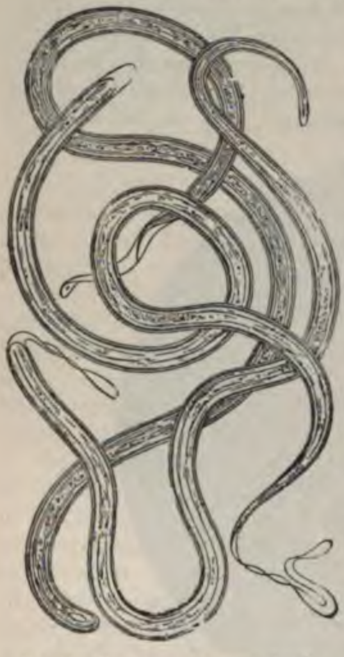

FIG. 55.—*F. nocturna*, showing sheath. After Lewis.

The filaria is enclosed in a delicate sheath (Fig. 55), which, being too long for it as it were, dangles from head or tail, or from both, giving rise to the appearance of a lash. The filaria can be seen to move backwards and forwards inside this sheath, which, as will be explained, is really the remains of the vitelline membrane of intra-uterine life. This organ subserves an important function in the life of the parasite—its object, if I may use the expression, being to act as a muzzle on the cephalic armature, and to prevent the parasite from using these formidable weapons prematurely; for if by means of them it penetrated the walls of the blood-vessels of the human host, and thereby escaped into the perivascular tissues, it would be out of the way of its intermediate host, and have no chance of continuing its development.

F. nocturna begins to appear in the peripheral circulation about five, six, or seven in the evening, and thereafter gradually increases in numbers up to midnight. After midnight the numbers diminish in the same gradual way as they had increased during the earlier part of the night. By seven or eight in the morning, save for an occasional straggler which may be encountered at any hour of the day, they have all disappeared. This remarkable phenomenon, which has been called "*filarial periodicity*," goes on daily and for years. It depends in some way on physiological conditions bound up with the sleeping and waking habits of the host; for if the latter sleep during the day and keep awake during the night, the filarial periodicity is correspondingly inverted. Fever and irregular habits of sleep are found to interfere with this peculiar phenomenon and otherwise to break up the regularity of its manifestations.

The number of filariæ discoverable in the blood at any given time will depend on the degree of infection of the individual, and also on the hour at which the examination is made. Under normal conditions the numbers in the circulation, as observed from day to day in the same individual, are found to be fairly uniform; but, as the parent worms may die as the result of accident or disease, and as the stock of parent worms may from time to time be increased, in the course of years the numbers of embryos free in the blood may fluctuate — increasing, or decreasing, or disappearing altogether. In blood drawn late in the evening—ten to twelve o'clock—it is no unusual thing to find as many as 100 parasites in a single drop, sometimes as many as 500. Assuming the filariæ to be uniformly distributed throughout the blood of the body, this would give an aggregate of some 3½ millions in every pound of blood, or 40 to 50 millions in an average-sized man. Notwithstanding these enormous numbers, their incessant activity, and their by no means insignificant dimensions, the embryo filariæ do no harm whatever, and the host is as unconscious of this huge population in his vessels as he is of his blood corpuscles.

The nocturnal habits of the filaria are an adaptation to the nocturnal habits of one or more species of mosquito, the females of which act as its intermediate hosts. These insects imbibe the parasite when they suck in the blood of an infected subject, and thereafter the parasite undergoes a metamorphosis in the tissues of the insect. This metamorphosis is completed at the time when, in the normal progress of events, the latter deposits her ova on the surface of the water. When the mosquito has deposited her eggs she dies almost immediately, probably falling into the water alongside her eggs. It is presumed that when this occurs the filaria, by that time enormously increased in size and power and provided with an alimentary canal, passes into the water, and by this medium obtains access to the human stomach. Boring its way through this and through the intervening tissues of the body, it finally arrives in the lymphatics, where after a time it attains sexual maturity.

The principal steps of this metamorphosis consist, in the first instance, of the escape of the filaria from the sheath which, up to the time of the arrival of the worm in the stomach of the mosquito, had muzzled its cephalic armature. This is brought about by the thickening the blood undergoes as soon as it is swallowed by the insect. The gastric juices so act on the blood corpuscles that their hæmoglobin escapes into the serum, which thereby, probably assisted by absorption, is rendered more viscid, gummy, and clinging. In this state it arrests the sheath, as it were, and so enables the filaria to ram its way through. This condition and effect of blood viscid from escaped hæmoglobin is readily reproduced experimentally by chilling (not freezing) blood slides containing filariæ—by laying the slides on ice for a few hours, and subsequently warming them to 70° or 80° F. In blood so treated it is easy to observe the filariæ ramming the sheath and butting their way out, head first, just as they do under normal conditions in the stomach of the mosquito (Fig. 56). When the filaria has got rid of its sheath in this way its cephalic armature is unmuzzled, and is at once made use of by the parasite to bore its way through the insect's stomach and into the thoracic viscera, where, a few hours after the mosquito has fed, the migrated filariæ can be found in great abundance. Here for a time the parasite falls into a sort of passive larval condition, acquiring four lips and an alimentary canal. Finally it takes to growing with great rapidity, becomes furnished with a three-lobed arrangement at its caudal end, and exhibits great activity, swimming about freely when placed in water. It measures at this stage 1·58 mm. by 0·03 mm. This metamorphosis takes six or seven days to accomplish, its completion concurring with the deposition of her ova by the mosquito and her subsequent death. The forms intermediate between this stage—that in which, presumably, it enters the human stomach—and the mature worm, some three or four inches in length, found lying in the lymphatics, have not been traced.

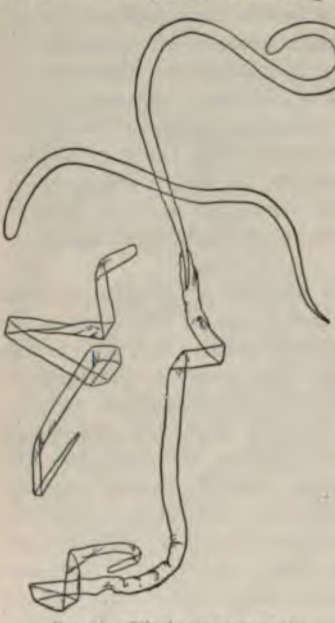

FIG. 56.—*Filaria nocturna* casting its sheath.

The mature *Filariæ nocturnæ* (Fig. 57)—named by Cobbold *F. Bancrofti*, after Bancroft of Brisbane, who, in 1876, was the first to find it—live in the lymphatics of the trunk and extremities. They have frequently been encountered in recent years, the sexes being usually found in association. Sometimes several—six or seven—are found together, coiled up and twisted about each other (Maitland); in other instances they appear to lie stretched out in the vessel containing them. When newly exposed they exhibit active wriggling movements, looking like short lengths of animated white horse-hairs. The males are particularly active, and show a great disposition to coil. These mature filariæ are long (female, 94 mm.; male, 70 mm.?), capillary (female, 0·185 mm.; male, 0·1 mm.), white, smooth, and uniform in thickness except near the head and tail, where they taper somewhat. The tail is incurvated in both sexes, spirally twisted like a vine tendril in the male, which can readily be recognised by the naked eye by this feature as well as by his inferior dimensions. The tail in both sexes is blunt at the tip, measuring there 0·03 mm. in breadth. In the female (Fig. 58, E) the anus opens 0·17 mm. from the tip of the tail, and the vulva about 1·2 mm. (?) behind the mouth. In both sexes the head is club-shaped, the mouth being terminal and simple (Fig. 58, C). The thick-lipped cloaca of the male is placed about 0·13 mm. from the tip of the tail (Fig. 58, A *c*). He has probably four pairs—not yet seen, however—of pre-anal papillæ; at least three pairs of post-anal papillæ have been made out. He has also

FIG. 57.—*Filaria Bancrofti*, female (nat. size). After Cobbold.

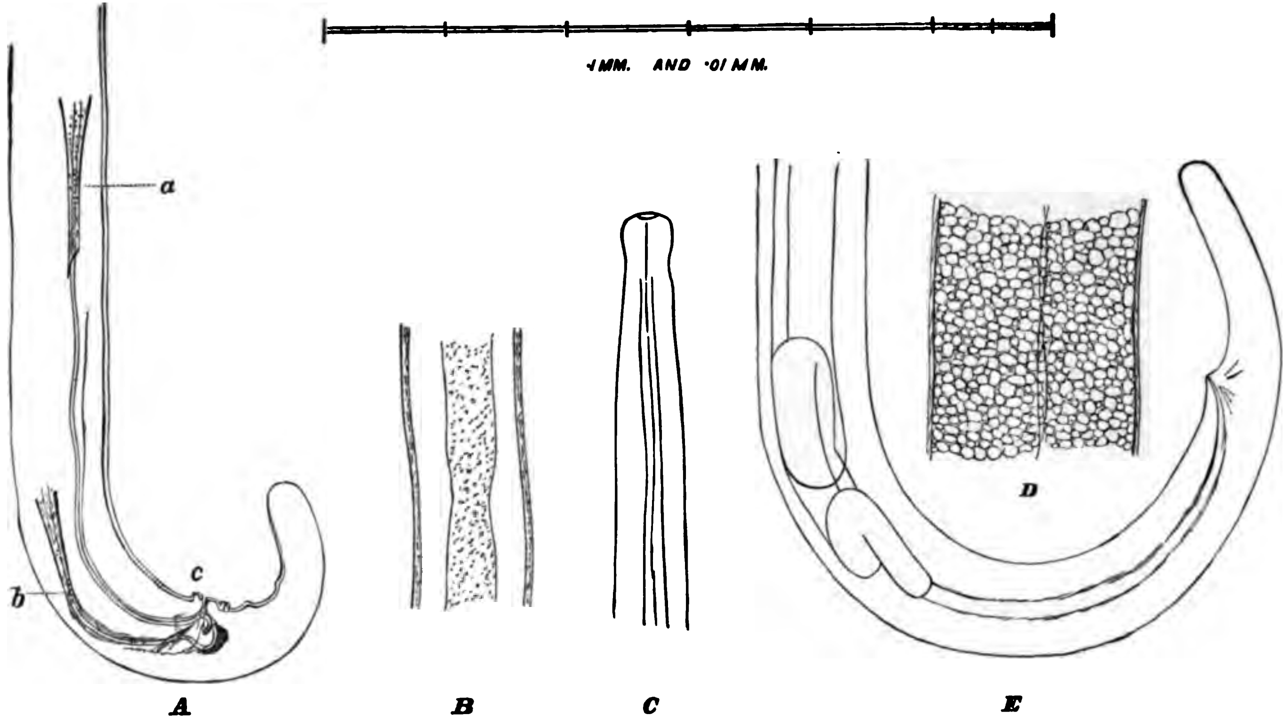

Fig. 58.—*Filaria Bancrofti* magnified. A, tail of male; B, constriction at junction of intestine and œsophagus; C, head and neck; D, fragment of female, showing uterine tubes; E, tail of female.

two unequal spicules (*a b*) (in length 0·6 and 0·2 mm. respectively) having rather broad, brownish-coloured, chitinous bases (length, 0·17 and 0·12 mm.), from which spring long, delicate, wavy, filamentous rods. The uterus is double (Fig. 58, D). The alimentary canal is simple and straight. The junction of œsophagus with intestine is said by Cobbold to be marked by a dilatation; in the several specimens which I have had the opportunity of examining I failed to find this dilatation; it seemed to me in one instance that the union, on the contrary, was marked by a constriction (Fig. 58, B). It is believed from the analogy of the corresponding blood-worm of the Chinese crow—*Corvus torquatus*—that in the higher part of the uterine tubes the differentiated embryos lie coiled up in the ova in the usual way, the ovum measuring at this stage 0·05 mm. by 0·034 mm.; that lower down the embryos have, by their incessant movements, so separated the poles of the ovum that the ovum becomes a long oval; and that still lower down, and near the vulva, the vitelline membrane has become so elongated by a continuation of this stretching process that it now constitutes the sheath of the free-swimming hæmatozoal filaria.

The young filariæ are born into the lymph which bathes the parent worm; in this they are carried along the lymphatics, traverse the glands (should any of these intervene), and, entering the thoracic duct, thus reach the blood. It is conjectured that if their arrival occurs during the night they circulate with their brethren; but if they should happen to enter the circulation during the day, after one or more rounds of the vessels, they are arrested for the time being, in some unknown organ or tissue, and in some unknown way.

Filariasis.—*F. nocturna*, both in its embryonic and in its mature forms, seems to be perfectly adapted to live in harmony with its human host. As a matter of fact, in the vast majority of instances it gives rise to no disease whatever. In some cases, however, this harmony is somehow interrupted, and then grave disease may accrue.

The endemic forms of a group of diseases—including chyluria, varicose groin glands, lymph-scrotum, chylocele, certain varieties of lymphorrhagia, orchitis, endemic lymphangitis, and varieties of cellulitis—all depending on a varicose condition of the lymphatics, are certainly attributable to *F. nocturna*. Endemic elephantiasis arabum is probably dependent on the same cause. For convenience I shall designate the former group "elephantoid diseases," the latter "elephantiasis."

ELEPHANTOID DISEASES

Chyluria.—Although at long intervals cases of chyluria originating in temperate climates, and in individuals who have never visited warm countries, have been reported, the vast majority of cases of this affection occur in persons who are living in or who have lived in tropical countries. There is scarcely a tropical country in which such cases are not encountered from time to time. Brazil, Mauritius, India, China, and the West Indies might be specified as supplying many of the recorded cases.

Both sexes are liable to the disease. In the case of women its first appearance may date from a pregnancy; in the case of men very often from some unusual physical effort. In many instances the symptoms supervene without manifest exciting cause.

Symptoms.—The characteristic symptom of chyluria—the milky condition of the urine—appears suddenly. On passing water the patient notices the peculiar alteration in its character; or, it may be, he is seized with retention, and when relief is obtained by the catheter, or spontaneously, after some hours of suffering, it is observed that the urine is opaque, milky white, pinkish, or red like blood. It is also remarked that it contains coagula, the intravesical formation of which had caused the retention. This condition of urine may persist for a day or two, for weeks, for months, or even for years. In most cases after a time the secretion becomes normal. But ever afterwards, at uncertain intervals of weeks, months, or years, the chylous condition is liable to recur, and to persist for an uncertain time.

Usually a relapse is preceded by a dragging, aching sensation in the loins, groins, thighs, testes, and about the pelvis generally. These uncomfortable sensations may disappear with the appearance of the chyluria; but if the abnormal discharge persist for a very long time this loin ache is apt to reappear, and to have superadded to it feelings of weakness, prostration, and all the usual symptoms of anæmia, including, very often, extreme mental depression.

In a certain proportion of cases of chyluria the glands of the groin are found to be prominent and varicose; the lymphatics of the scrotum may be similarly dilated. The colour of the urine and the amount of clot it contains vary in different cases, and even in the same case at different times of the day, and from day to day. In some instances the urine may be milky white; usually it has a pinkish tinge; in yet other cases it may be red like blood. The latter condition is sometimes called "hæmato-chyluria." Generally the urine passed on rising in the morning is to all appearance normal, and it is only as the day wears on that it becomes chylous. In other cases the morning urine is chylous, whereas the urine passed at some other time of the day may be quite, or almost, clear. In some cases clots are formed in the bladder, giving rise to pain and difficulty in passing water; in other cases the coagulum is not formed till the urine has left the body; and in another class of cases no coagulum forms at all, or only occasionally.

Usually, if chylous urine is passed into a urine-glass, the entire mass of fluid coagulates rapidly. In a very short time the clot thus formed contracts, becoming, as it contracts, pinker or redder in colour, firmer and more fibrous in consistence; the fluid in which it floats looking whiter and clearer in contrast. In the course of a few hours, or of a day, the coagulum contracts to comparatively small dimensions. The fluid portion of the urine has now separated into three layers—an upper, forming a thin, greasy, cream-like layer or pellicle; a lower, formed of scanty, dark-red sediment; and an intermediate layer, constituting the bulk of the fluid in which the coagulum is suspended. Under the microscope oil globules and much granular fatty matter are to be found in the upper layer; in the middle layer much molecular fatty matter and some lymph and blood corpuscles; and in the lower layer a larger proportion of lymph and blood corpuscles, besides small clots, urinary salts, and epithelium, and, in the majority of instances, dead or slowly moving embryo filariæ. If a portion of the clot be teased up it is found to contain, enclosed in the meshes of the fibrine, lymph corpuscles, red corpuscles, and, in most cases, a considerable number of filariæ.

To find the filariæ in the urine it is necessary to employ a low magnifying power, 50 to 80 diameters; and to search in the sediment or in the clot. To search in newly-passed urine, or in the upper and middle layers above referred to, is almost a hopeless task.

On shaking the urine up with ether it becomes clear; on boiling it large quantities of albumin are thrown down.

Judging from a limited number of observations the filaria does not exhibit in the urine that diurnal periodicity which characterises it in the blood; it may be found in chylous urine at any hour, irrespective of the time at which the urine was voided. So far as known, if the filaria be found in the urine it will also be found in the blood, that is, if searched for at the proper time.

Chyluria, although often an extremely debilitating disease, is seldom directly fatal. Connected, as it usually is, with the presence of mature parasites in the thoracic duct, it is liable at any moment to be complicated by serious conditions arising out of the death of one or more of these parasites. Generally no bad consequences result from the death of the parent filariæ, but there is evidence that at times such an event may be the starting-point of a septic abscess which, being located in a surgically inaccessible position, may prove fatal.

Diagnosis.—The presence of clots at once distinguishes chyluria from such purulent conditions of urine as are associated with pyelitis, abscess rupturing into the urinary tract, and cystitis; and from phosphaturia, etc. Diagnosis is further aided by the discovery of filariæ in the urine and blood, by varicose conditions of the groin lymphatics, and other symptoms of filariasis. The only condition about which doubt might be entertained is a combination of chyluria with endemic hæmaturia. The concurrence in the urine of filariæ and bilharzia ova will at once clear up the difficulty. It sometimes happens, however, that the filaria has disappeared; in such a case diagnosis may be difficult if not impossible.

The pathology and treatment of chyluria will be given under Urinary Diseases (vol. iii.)

Varicose inguinal glands is a very common effect of the presence of *F. nocturna* in the lymphatics. Both groins may be involved, usually one side more than the other; occasionally one side only is affected.

On inspection the upper part of Scarpa's triangle is seen to be occupied by a rounded, obscurely lobulated, broad-based swelling, suggesting hernia. In many instances the swelling has the appearance of being made up of two main masses—an upper, roughly corresponding to the direction of Poupart's ligament; and a lower, corresponding to the saphenous opening. These swellings, which merge into each other, may attain the size of one or two fists, or they may be no larger than a small apple or a walnut. To the touch they are doughy, obscurely fluctuating, with perhaps here and there harder kernel-like masses. In other instances the swellings are firmer, and very obscurely varicose. The superjacent skin is freely movable, but the tumour cannot be slipped over the subjacent tissues; in the recumbent position the swelling diminishes considerably; firm pressure disperses it altogether. Still keeping the palm of the hand on the affected region, if the patient be made to stand up, the swelling slowly returns, contrary to what would happen in hernia; and on percussing it the note is found to be dull, not tympanitic as in hernia. In coughing there may be a slight impulse, but this is not nearly so marked as in hernia. When taxis is made in the recumbent posture, though the swelling disappears, it does so very slowly; there is no sudden slipping up of the mass or attendant gurgling, as in hernia. It will be seen that the characters of the tumour approximate more to those of an epiplocele than of an ordinary hernia.

If a hypodermic needle be thrust into the tumour a syringeful of opaque milky, or pinkish, or sanguinolent, or straw-coloured fluid can be readily withdrawn; and if the barrel of the syringe be laid aside, the needle remaining in place, the fluid will continue to drop from it for hours, and until many ounces have escaped. On withdrawing the needle some swelling may arise around the tumour, apparently from infiltration of the fluid into the cellular tissue; this, however, is quickly absorbed, and the swelling in a few hours reverts to its usual size.

The aspirated fluid coagulates rapidly. Under the microscope it is found to contain much molecular fatty matter, lymph, blood corpuscles, and generally, though not invariably, very active filariæ.

These tumours are said by Mazaé Azéma to appear, as a rule, between the thirteenth and twentieth years, and to tend to disappear between forty and fifty; of this I have no experience. From time to time they may be the seat of periadenitis and are then very painful. As a rule, however, beyond a sense of distension and dragging, generally much increased by exercise and the erect posture, and then often exceedingly distressing, they are not attended with actual pain.

It is a rare thing to meet with a similar affection of the axillary glands, although a few such cases have been recorded.

Lymph-scrotum, like chyluria and varicose groin glands, is almost a sure indication of the presence, actual or past, of *F. nocturna* in the lymphatics.

On inspecting and palpating such a scrotum it is found to be slightly or very considerably enlarged and perhaps thickened. Here and there, scattered over the surface, sometimes arranged in lines or groups, herpes-like but non-inflammatory vesicles, varying in size and number, Autopsy has shown that in varicose groin glands the tumour consists of a mass of dilated lymphatics which are but part of an enormous varix extending into the pelvis and involving the thoracic duct. Two valuable autopsies of cases of chyluria associated with the filaria made in recent years—one by Dr. Stephen Mackenzie, the other by Prof. Curnow—revealed in both instances an impervious condition of the upper part of the thoracic duct, and enormous dilatation of that vessel below the seat of obstruction, together with a varicose condition of the abdominal, renal, and pelvic lymphatics. These facts, together with the circumstance that the milky fluid in the urine in chyluria, in varicose groin glands, in lymph-scrotum, and in chylocele possesses all the characters of chyle plus the presence of filaria embryos in the fluid as in the blood, have led me to advance the following theory of the production of these diseases:—

In some way as yet unexplained, either by mechanical plugging by a bunch of intertwined parent filariæ, or in consequence of inflammatory conditions brought about by the presence of the filaria in the vessel and leading to stenosis, or in some other way connected with the parent filariæ, the thoracic duct becomes occluded. As a result of this occlusion there is stasis of chyle and lymph in the thoracic duct and in all its tributaries below the point of obstruction. Concurrently with the stasis there is a rise of pressure in the lymphatics of the implicated area. As a consequence of this rise of pressure, a movement of lymph sets in the direction of least pressure, that is, towards the anastomosis of the lymphatic system of the thoracic duct with the lymphatic system draining the upper part of the body. The relief thus obtained will gradually extend nearer and nearer to the thoracic duct itself, and finally the contents of this vessel will partake in it. But for the contents of the thoracic duct—which include the chyle from the intestine—to reach this anastomosis they must take a recurrent course, through the pelvic lymphatics, through the inguinal and upper femoral lymphatics, through the scrotal lymphatics, and so over the abdomen and back to the upper part of the body. To accommodate this augmented stream these lymphatics must dilate; this, together with the rise in pressure which must accrue before the anastomosis is completed, may end in producing a varix which, should it involve the renal or vesical system of lymphatics, may by rupture give rise to chyluria; if it include the inguino-femoral glands—varicose groin lymphatics; if the scrotum—lymph-scrotum; if the tunica vaginalis—chylocele.

If this theory be not correct, how can the presence of chyle in the urine, in the groin, in the scrotum, and in the tunica vaginalis be explained? Chyle must come from the lacteals, and the only route by which it can reach these parts is the one described. When we tap a lymphatic varix of the scrotum or of the groin, we tap the anastomotic plexus by which the chyle, denied a route up the thoracic duct, is finding its way to the circulation.

Objection has been raised to this supposition on the ground that the abnormal substance in the urine in chyluria is sometimes sanguineous, and therefore that it must have come, in part at least, from the blood-vessels; and impossibilities, such as perforation of the blood-vessels, have accordingly been attributed to the embryo filariæ. But in a certain proportion of cases these embryos are wholly absent from the urine and also from the blood; and yet the so-called hæmato-chyluria persists for years. If, then, in some cases the sanguineous character of the urine arises independently of embryo filariæ, why not in all? It is a well-known fact that in the upper part of the thoracic duct the lymph is pinkish, sometimes even red; and includes some red blood corpuscles. This is specially noticeable in dogs which have survived ligature of the thoracic duct for some time. Manifestly the contents of this vessel, even if delayed in the vessel, continue their normal evolution towards the formation of blood. Thus, without assuming rupture or perforation of blood-vessels, the pinkish or red tinge and the red corpuscles in some cases of chyluria can be satisfactorily explained. These diseases are entirely diseases of the lymphatic system; the blood-vessels are not engaged in them.

After obstruction of the thoracic duct has been set up by the parent filariæ, it is of no consequence, so far as the production of an inverted flow of chyle and lymph is concerned, whether the filariæ live or die. A stricture of this description once produced is permanent, and continues after the cause which had given rise to it has long passed away. Hence the occasional absence in chyluria, and in the other forms of lymphatic varix described, of the embryo filariæ. In such cases the parent filariæ, after having damaged the thoracic duct, had died.

Elephantiasis arabum.—Although elephantoid thickening of the integuments of the feet and legs and of other parts occasionally originates in cold climates, such an occurrence must be considered as extremely rare. In the tropics and subtropics it is otherwise. There elephantiasis is common enough—in some places so common that a large proportion of the inhabitants are affected. For example: in parts of Travancore about every twentieth individual has elephantiasis; in some of the South Pacific Islands (Samoa, Huahine) nearly half the inhabitants are affected. These are extreme cases; but almost everywhere in the tropics this disease is more or less common. It becomes rarer as we proceed north and south; beyond the 35th degrees of N. and S. latitudes it is practically unknown.

Elephantiasis affects various regions of the body. As a rule the legs or scrotum, or both, are the only parts attacked; at times, however, the disease shows itself in the arms, in the mammæ, and in the female genitals.

According to statistics prepared from 2081 cases occurring in India and Brazil, the following parts, alone or in conjunction with other regions of the body, were affected in the percentages stated:—Lower extremities, 96·84 per cent; upper extremities, 5·86 per cent; scrotum, 2·3 per cent. The mammæ were involved once in every 690 cases; the lobe of the ear only once in the entire series. No mention is made in these statistics of the disease attacking the female genitals. It would appear that in districts in which the endemic influence is very powerful the proportion of arm, scrotum, and mammæ cases to leg cases is greater than in districts in which the endemic influence is milder; thus in the South Pacific Islands arm and breast cases are not infrequent.

Elephantiasis begins with an attack of lymphangitis and erysipelatoid inflammation of the integuments. Constitutional symptoms are severe, setting in with a sharp and prolonged rigor, followed by high fever, which, in the course of a day or two, generally ends in profuse diaphoresis, and often in a sort of lymphous weeping from the implicated skin. The inflammatory effusion is only partially absorbed, some thickening remains. These attacks recur at irregular intervals of weeks or months, each attack leaving the limb or scrotum somewhat larger than before, until, in the course of years, the skin and cellular tissue has become enormously and permanently hypertrophied, and an unwieldy mass, justifying its name—elephant leg, is formed.

In the long-established disease the surface of the affected part is rough and tuberose, the papillæ pilose, warty or atrophied. At the ankle—if it be the leg that is affected—the skin is thrown into folds like rhinoceros hide, deep sulci between the folds permitting a small range of movement at the joint. The nails are rough and thick; the hairs, in parts, long and coarse; sensation is somewhat impaired; sweating is defective, and the parts are often darker than normal. Usually in the case of the leg the disease does not extend above the knee, although instances of implication of the thigh are by no means rare; in the latter case folds and sulci around the joint permit some degree of motion. The margin of the diseased patch may be rather abruptly defined, or it may pass gradually into sound skin.

When the scrotum is affected the tumour assumes, as it enlarges, a pyriform shape, the neck of the swelling being towards the pubes. The penile integuments, as a rule, are dragged down into the mass, so that the penis becomes buried at the upper part, the glans lying at the bottom of a long tunnel which opens half-way down, or even lower, on the anterior surface of the tumour. Sometimes the integuments of the penis are specially affected, and then they form a long ram's-horn-like projection springing, as it were, from the face of the mass. In all cases the testes are dragged down in consequence of the fibrous attachment they have to the bottom of the scrotum through the remains of the gubernaculum testis; consequently the cords are very much elongated. Frequently the testes carry large hydroceles; very often they are deformed or atrophied by pressure.

In the case of the legs a girth at the calf of from 10 to 24 inches, and in the case of the scrotum a weight of from one to two pounds up to 50, or 100, or even 200 pounds, may be attained. An average measurement for a leg in a state of elephantiasis would be 11 to 12 inches; an average weight for a scrotal tumour 10 to 30 pounds. The skin of the mammæ, when this organ is attacked, may enlarge till the nipple hangs as low as the umbilicus or pubes; cases are on record in which the mamma reached the knee and weighed many pounds. Labia weighing seven or eight pounds have frequently been removed.

Circumscribed patches of elephantised integument are not uncommon. Recently Corney and Daniells have described such patches as being frequent among the Fijians, in whom, when they affect the skin over Scarpa's triangle, they eventuate in massive pear-shaped tumours many pounds in weight.

On cutting into the affected tissues in elephantiasis the derma and external layers of the subcutaneous areolar tissues are found dense, white, fibrous, and enormously thickened—perhaps attaining a thickness of from one to two inches—particularly in the scrotum. The deeper part of the superficial fascia is converted into a loose, yellowish, blubbery-looking dropsical tissue containing here and there fibrous bands and many large veins and lymphatics. The sheaths of the large vessels and nerves, and the muscular aponeuroses are thickened; the underlying bones may also be hypertrophied and rough. The lymphatic trunks are dilated, and their radicles varicose and thinned.

In all cases the lymphatic glands are enlarged, dense, and fibrous; and not the glands of the affected side only, but often those of the opposite limb also.

Ulcers sometimes form on the affected limbs, and in the larger scrotal tumours large abscesses and even gangrenous patches are not uncommon.

Apart from the risks attending secondary septic conditions arising from such mishaps, elephantiasis, though painful when inflamed, and cumbersome at all times, is not a disease involving much danger to life.

Pathology of elephantiasis.—The pathology of elephantiasis is still obscure. Although there is sufficient evidence to connect it with *F. nocturna*, the exact way in which the parasite brings about the lymph stasis, which pathologists agree to be the main factor in the disease, is still a matter of speculation.

The following are the principal grounds for incriminating the filaria: (*a*) The geographical ranges and the degrees of prevalence of elephantiasis and *F. nocturna*, so far as we know, correspond. (*b*) Elephantiasis is a disease essentially of the lymphatic system; the filaria, in its mature form, is essentially a parasite of the same system. (*c*) Elephantiasis frequently accompanies or supervenes on the elephantoid diseases. (*d*) The elephantoid diseases—themselves diseases of the lymphatic system—are generally associated with a peculiar type of fever and inflammation; the same type of fever and inflammation is always a feature in the development of elephantiasis. (*e*) Seeing that elephantoid diseases have been proved to be caused by the filaria, it is reasonable to conclude that elephantiasis is brought about by the same parasite.

There are certain cases of lymph-scrotum and of varicose groin glands in which the contents of the lymphatic varix are clear and lymphous, and not, as is usually the case, chylous. Manifestly such contents come from leg or scrotum only, and are not, in such instances, a regurgitation from the intra-abdominal lymphatic system. Sometimes in these cases filaria embryos are found in the lymph from the varix although they cannot be found in the blood. The inference from this fact is that the lymph containing the parasite cannot reach the circulation, otherwise the filaria would be discoverable in the blood. On two occasions, in examining the lymph in such cases, I encountered large numbers of ova, filaria ova, measuring $\frac{1}{500}''$ by $\frac{1}{725}''$. In this circumstance I believe the explanation of the pathology, not only of the particular class of varix in which these ova occurred but also of elephantiasis, is to be found.

The filaria is normally viviparous. Its young, when born, are long, outstretched animals possessing the power of independent movement, and to a certain extent of locomotion. Though long they are no broader than a red blood corpuscle, and therefore can pass wherever red blood corpuscles can pass. But the ova of the filaria are very much broader bodies; they are passive, and therefore incapable of contributing to their own passage through the vessels.

The fact that ova were found in lymph proves that the process of parturition in the filaria from which these particular ova proceeded had been morbidly hurried; in other words, the contents of the parasite's uterus had been discharged before the intra-uterine development had been completed, before the spherical ovum had been converted into the elongated embryo.

The effect of such an occurrence on the lymphatics in which the mature filaria lies may be imagined.

Under normal conditions the young filariæ proceeding from a parent worm traverse the lymphatic glands without difficulty; but should an injury to the female filaria—an event very likely to occur in so exposed a situation as the leg — cause her to abort—to empty her uterus prematurely—then, instead of the long, slender, sinuous, active embryo, the broad, passive, spherical ova from the upper end of the parasite's uterus will be launched into the lymph-stream. These ova will be carried to the nearest lymphatic gland, and, being too large to traverse these vessels, will plug the entire system of afferent vessels appertaining to this gland. Then the anastomosis will carry the arrested and diverted ova-bearing lymph-stream to the next gland. This gland will be plugged in turn; and so on until the entire lymphatic system connected directly or by anastomosis with the vessel in which the aborting filaria lies is completely cut off from the circulation. A slight blow, or wound, or septic inoculation would readily set up inflammation in such a congested area and elephantiasis will be established.

Objection has been raised to this hypothesis on the ground that filariæ are rarely found in the blood in elephantiasis. This objection is readily answered by the consideration that the very circumstances and mechanism by which the filariæ bring about the disease prevent their embryos from appearing in the blood; these cannot traverse the occluded glands any more than the lymph can.

It is a curious and significant circumstance that in a country in which both elephantiasis and the filaria are extensively endemic, filariæ are found very much more frequently in individuals who are not affected with elephantiasis than in persons who are so affected. Thus in 88 blood-slides received from Cochin, 74 came from healthy individuals—in these 74 slides filariæ were found in 20, or in about 1 in 3·7; 14 came from cases of elephantiasis, but in only 1 of these 14 slides were filariæ found. These figures not only prove the great frequency of the filaria in countries in which elephantiasis is extensively endemic, but they are a powerful support to the opinions offered concerning the particular way in which the parasite brings about this disease. In such countries filariæ are less likely to be found in those persons who are affected with elephantiasis than in those who are not, seeing that in the former the lymphatic system of a considerable part of the body is blocked. But in countries in which the filaria is still more prevalent—in which, presumably, every sound man and woman carries the parasite, in such countries even those inhabitants in whom a part of the lymphatic system is blocked, if on the other hand in them a small part of this system remains patent and connected with the circulation, such is the prevalence of the filaria that even those affected with a moderate area of elephantiasis may have the filaria circulating in the blood. Thus of 56 slides of night blood, from 56 cases of elephantiasis and elephantoid conditions, which Dr. Davies collected for me in Samoa, no fewer than 27 contained the filaria, many of them in great profusion.

Many other hypotheses of the causation of elephantiasis have been advanced from time to time, but none of them explain or, indeed, are compatible with all the facts now ascertained about this disease.

Treatment of Filariasis.—No means have been discovered of killing the filaria in the body, and as it is impossible, with rare exceptions, to localise it with sufficient precision, excision of the parent worms is usually out of the question. The only way to secure immunity from filarial disease in the endemic region is by a prophylaxis, founded on our knowledge of the life-history of the parasite. Drinking-water must be beyond suspicion. If necessary it should be boiled or filtered, and the vessels in which it is stored ought to be protected by a fine-meshed wire-gauze covering to keep out mosquitoes. The subjects of filarial infection should be made to sleep below mosquito-netting, and never near the water-supply of a family or community.

Persons known to harbour filariæ ought to avoid blows and injuries of all kinds, and every circumstance which might cause the parent filariæ to abort, or which might set up lymphangitis in congested lymphatic areas.

The pathology of the various forms of filarial disease indicates their special treatment.

Chyluria is best treated on mechanical principles, effort being directed to lessen the pressure on the vessels of the leaking renal or vesical lymphatic varix. The recumbent position with raised pelvis should be maintained until the urine becomes clear and free from clot and albumin.

All foods likely to increase the amount of chyle, such as fats and albuminoids, should for a time be avoided, and the amount of fluid restricted as much as possible. By following such a dietary the chylous appearance in the urine often disappears in a day or two. This does not mean cure, however, in every case; for if we inspect the urine carefully we can still, and for a longer or shorter time, see floating in it a lymphous clot, and on boiling find it loaded with albumin. So long as clot and albumin are present, the leak in the lymphatic varix is not healed, although the fatty matter, not being supplied to the chyle, may not be present. A single tumblerful of milk will at once give ocular proof of the patency or otherwise of the rupture in the varix. Not until clot and albumin have entirely disappeared, and the milk test gives a negative result, should the patient be allowed to quit the recumbent position.

It is well to give a saline aperient from time to time. I have tried many other drugs which have been recommended, including benzoic acid and the benzoates, gallic acid, the salts of iron, glycerine, mangrove bark, chromic acid, thymol, salicylate of soda, and so on, but I cannot say that I have seen benefit from any of them. In judging of the value of a remedy in this disease it must always be borne in mind that every now and again chyluria ceases spontaneously; the drug which was being taken when the chyluria so ceased is apt to be credited with the cure.

Varicose inguinal glands ought to be left alone or gently supported by a well-adjusted bandage. If they are so painful and so tense that the patient is thereby disqualified from making a living, the question of their excision might be entertained. But the surgeon must not forget that these dilated lymphatics are part of a physiologically necessary varix. Their excision has been followed by chyluria and also by elephantiasis, and once or twice with benefit which appeared to be permanent (Maitland). In a case recently operated on by Mr. Johnson Smith, the lymphatics of the right spermatic cord subsequently became enormously dilated and caused much pain and inconvenience.

Lymph-scrotum.—The same remarks apply to this as to the preceding case. When passing into confirmed elephantiasis a lymph-scrotum ought to be excised.

Chylocele may be tapped and injected or incised.

Elephantiasis of the scrotum should be amputated, the penis and testes being retained.

Elephantiasis of the leg is best treated by rest, elevation, massage, and elastic bandaging. If of recent formation, and the patient sound in constitution, and neither malarious, anæmic, nor scorbutic, a mild mercurial course may be beneficial. During acute attacks pricking the distended limb so as to provide an escape for the effusion, and dressing the parts antiseptically, gives great relief, and may tend to delay the progress of the swelling. Pain and fever are to be treated on general principles.

Filaria Magalhaesi.—Recently Professor Magalhaes, of Rio de Janeiro, has published a careful description of two sexually mature filariæ which were found in a clot of blood said to have come from the left ventricle of the heart of a child. The disease of which the patient died is not stated. The female measured 155 mm. in length by 0·71 mm. in greatest breadth, the male 83 mm. in length by 0·4 mm. in greatest breadth. Both were white, opalescent, and delicately marked by transverse striæ. In both the œsophagus terminated in a bulb, the intestine commencing in a dilatation; and in both the head was club-shaped, and the mouth terminal, round, simple, and without papillæ. In the female the vulva was placed 2·56 mm. from the mouth, the uterus was double, and the anus opened 0·13 mm. from the tip of the rounded tail. The male was provided with two spicules projecting from the cloaca, 0·11 mm. from the tip of the rounded tail, which was further provided with four pre-anal and three post-anal pairs of papillæ. We have no description of the embryos, which, it is to be presumed, must have circulated in the blood. Judging from the measurements, the character of the spicules, and the position in which these worms were found, I believe that they were not *Filariæ Bancrofti*, the parental form of *Filaria nocturna*, and I have suggested, on geographical grounds, that they may turn out to be the parental forms of a nematode embryo which I have recently found in the blood of certain West Indian negroes.

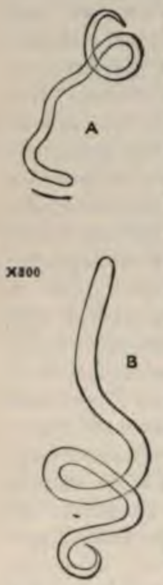

Fig. 59.—A, *F. Demarquaii.* B, *F. nocturna* (× 300). Drawn from slides prepared in the same way.

Filaria Demarquaii.[1]—Some time ago Dr. Newsam of St. Vincent, W.I., kindly sent me some specimens of dried blood from 152 natives of that island. Several of the slides contained the ordinary *Filaria nocturna.* In certain other slides, prepared from ten individuals, an embryo nematode was found which differed so much in size and in periodicity from *F. nocturna* that it is almost certain it belongs to an entirely different species. These new hæmatozoa are sheathed and sharp-tailed like *F. nocturna*, but differ from this hæmatozoon, inasmuch as they occur in day blood as well as in night blood, and moreover are very much smaller. As all the specimens perceived were dried in postures more or less contorted, it is impossible to give accurate measurements. A comparison of the accompanying figures, carefully drawn to scale, and from preparations made in the same way, will convey some idea of the relative dimensions of the new blood-worm and *F. nocturna.* Until the parasite is examined alive, and in newly-drawn blood, further particulars cannot be ascertained. I think I have met with the same hæmatozoon in dried specimens of blood sent to me from the River Niger region by Dr. Crosse.

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[1] I have named this new blood worm *Filaria Demarquaii*, at Professor Blanchard's suggestion, after Demarquay, the discoverer of *Filaria nocturna*, and therefore the pioneer of this important branch of pathology. Demarquay was a native of the West Indies; there is, therefore, a certain appropriateness in calling this West Indian parasite after him, as well as being a recognition of scientific services too long overlooked even by his own nation.

The individuals supplying these St. Vincent filariæ are said to be healthy.

The subjoined table gives the results of a series of systematic examinations of blood from natives of different parts of the world. It may be of use as an index to the forms of blood filaria indigenous to the regions it refers to, and it may convey some idea of the extent to which these parasites prevail in some parts of the world. Statistics prepared prior to the discovery of filarial periodicity and of the newer *Filariæ sanguinis* are fallacious :—

Locality.	Sent by	No. of individuals supplying blood slides.	Day or night blood.	Species of parasite and number of slides it was found in.			
				Filaria nocturna.	Filaria diurna.	Filaria perstans.	Filaria Demarquaii.
Congo Lukunga	Dr. Wolfrideson	14	Day	0	0	9	0
Banza manteka ; San Salvador	Dr. Small	61	Day	0	0	35	0
Old Calabar	Mr. R. Henshaw	27	Both	1	1	15	0
Cochin-India	Surgeon-Major Eleum	88	Night	21	0	0	0
South Africa	Dr. Burns	74	Both	0	0	0	0
Zanzibar	Dr. Burns	1	Both	1	0	0	0
Samoa	Dr. Davies	56	Night	27	0	0	0
St. Vincent, W.I.	Dr. Newsam	152	Both	6	0	0	10
Dahomey	Crystal Palace, London	49	Both	2	1[1]	0	0
Lower Niger[2]	Dr. Crosse	53	Day	0	0	3	5?

Family—Anguillulida

This family is represented in man by one species only. This belongs to the genus rhabditis, the members of which are characterised by a minute filiform body tapering towards both ends, a sharp-pointed tail, and a rounded-off head carrying a terminal mouth ; the œsophagus has two bulbous swellings, the more posterior of which is furnished with three tooth-like folds ; the symmetrical double ovaries are straight ; the male has two spicules, and usually a copulatory bursa with from six to ten papillæ.

Rhabditis Niellyi.—Prof. Nielly, of Brest, has described a case of skin disease, characterised by a papulo-vesicular eruption attended with intense itching, in the vesicles of which an immature rhabditiform parasite—0·335 by 0·013 mm.—was discovered. The double-bulbed œsophagus was well developed, but the genital organs were quite rudimentary; evidently the animal was immature. In the same patient's blood a number of free embryo nematodes were found, suggesting that the mature parental form was lodged somewhere in the tissues and in connection with the circulation. Possibly the embryos, after circulating for a time in the blood, escaped from the vessels and became lodged under the skin, where, on attaining a certain degree of development, they set up an irritation which induced scratching and led to their liberation. Thus, possibly, they were placed in a position to advance further towards maturity—perhaps in the body of an intermediate host—before finally gaining access to the body of the definitive host, where they might attain to sexual maturity. Similar forms of parasitism are found in the lower animals, and it is probable that *R. Niellyi* is normally a parasite of some of these.

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[1] The interpreter of the troupe and a traveller.

[2] Employed by the Niger Company and coming from various parts of West Africa.

O'Neil has described, under the name "Crawcraw"—which means in the native languages simply itching skin disease—an itching papulo-vesicular skin affection very similar to that described by Prof. Nielly, and similarly characterised by the presence of immature nematodes in the papules of the skin lesion. I have suggested, considering the geographical distribution of the two parasites, and the peculiar structure and habits of *F. perstans*, that possibly the crawcraw nematode is an advanced developmental stage of the latter.

Family—Rhabdonemida

This family, like the preceding, also includes only one species parasitic in man. The various species are heterogamous, each species including a free, bisexual, and rhabditic form and a parasitic, filaria-like, and hermaphrodite form.

Rhabdonema intestinale—(Synonyms: *Anguillula intestinalis*, *Rhabdonema intestinale*, *Rhabdonema strongyloides*).—This parasite, discovered by Normand in 1876 in cases of chronic intestinal flux from Cochin-China, has since been found in many parts of the world—in Brazil, West Indies, Egypt, Ceylon, Italy, Germany, etc. I have seen it in Lascars coming from ships trading to Bombay. It is very often found in association with *A. duodenale*, and it is probable that the geographical range as well as the biological requirements of these two parasites are closely similar.

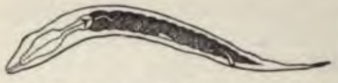

FIG. 60.—Embryo *Rhabdonema intestinale* in fæces. After Golgi and Monti.

The mature rhabdonema lives in the intestinal mucus of the duodenum and upper part of the jejunum; rarely in the stomach or ileum. It is a very minute and, proportionately, very long parasite—2 by 0·04 mm. It is readily distinguishable under the microscope from all other intestinal parasites by its size and proportions, and by the five or six ellipsoidal eggs (0·06 by 0·034 mm.) lying in a string about the centre of its body and in close relation to the position of the vulva. No male form has been found. When the ova have passed into the chyme the embryo (Fig. 60) develops so rapidly that before the fæces leave the intestine the shell of the egg has been ruptured and the embryo is swimming about very actively in the fluid fæces. These embryos have pointed tails, rounded heads, and measure 0·2 or 0·3 by 0·013 mm. They are further distinguished by the double œsophageal bulb, the posterior bulb of which carries three teeth. Unlike what occurs in the case of *A. duodenale*, owing to the rapid development of the embryo and its early escape from the ovum, ova are rarely found in the stools, unless it be during the action of a powerful cathartic. When they do occur in the stools, being usually in strings of three or four, they are not likely to be confounded with the ova of any other parasite.

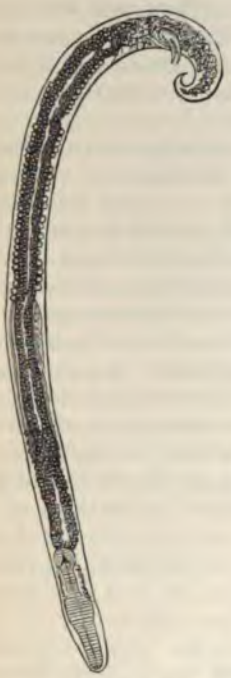

FIG. 61.—*Anguillula stercoralis*, male. Golgi and Monti.

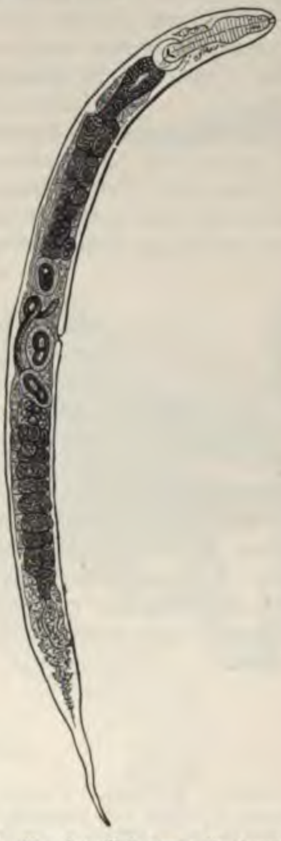

FIG. 62.—*Anguillula stercoralis*, female. Golgi and Monti.

The future of the embryos after they leave the human body depends on several circumstances. First, unless they get access to non-putrefying fluid they soon die; the fæces containing them, therefore, must mix freely with water. Second, if the temperature be low the embryo rhabdonema develops into a filariform larva which, when swallowed by man, quickly assumes the parasitic form already described. Third, if the temperature be high the embryos develop into male (Fig. 61) (0·7 mm.) and female (Fig. 62) (1·0 mm.) mature rhabditic worms. In due time these rhabditic forms produce embryos which assume the filariform type (Fig. 63) and, on being transferred to man, become *R. intestinale.* These free mature rhabditic forms are what were formerly known as *Anguillula stercoralis.* They were found in the fæces at post-mortem examinations, and also in the fæces after discharge; for a long time their true relationship to the *R. intestinale* was not understood.

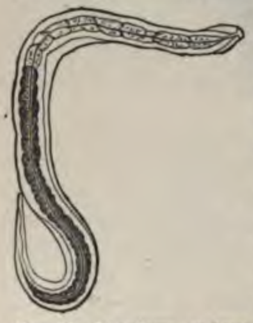
FIG. 63.—Filariform embryo of *Anguillula stercoralis.* Golgi and Monti.

At one time this parasite was supposed to be the cause of the diarrhœa so common in Cochin-China. This is no longer believed, and most pathologists regard the presence of the worm in these cases as more or less accidental—favoured no doubt by the catarrhal condition of the intestinal mucous membrane, but certainly not causing it.

Treatment.—*R. intestinale* is difficult to expel. Sonsino says he got good results from a long course of small doses of thymol and liquor ferri perchloridi. The ordinary anthelmintics are ineffective in the case of this parasite. Prevention must take the direction of a pure water-supply and the avoidance of uncooked vegetables. There is some evidence to show that the desiccated filariform embryos may gain access to the alimentary canal in the shape of wind-borne dust.

PATRICK MANSON.

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BILHARZIA HÆMATOBIA

RARELY seen in times past, the formidable train of symptoms caused by this hæmatozoon have of late, owing to the rapid peopling of Africa by Europeans, presented themselves frequently to English and French practitioners, especially to army surgeons. Larrey and his colleagues met with many cases of hæmaturia during Napoleon's Egyptian campaign, but failed to recognise the cause. Bilharz first discovered the parasite in 1851.

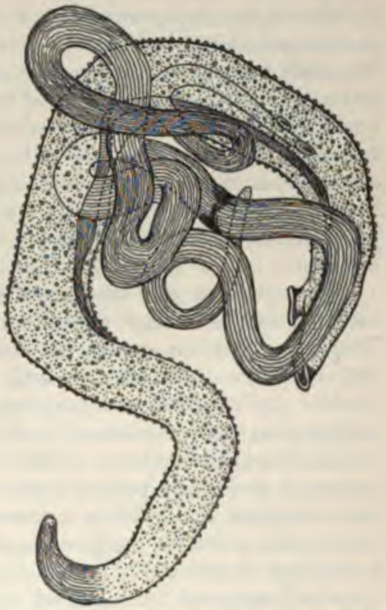

FIG. 64.—Male *B. hæmatobia*, with female partly enclosed in gynæcophoric canal. After Lortet and Vialleton.

Anatomy of Adult.—Bilharzia (*vel* Distomum, *vel* Gynæcophorus) hæmatobia is a trematode platyhelminth inhabiting the veins of man, monkeys, and probably also of cattle and dogs. The Distomidæ are for the most part hermaphrodite, but in this species the sexes are separate. The *male* is whitish (Fig. 64), from 7 to 16 mm. long (about $\frac{1}{2}$ inch); upper surface slightly convex and covered with minute ciliated tubercles; lateral margins of body flattened and bent so completely round as to overlap and form a ventral canal (the gynæcophoric canal), in which a portion of the body of the female lies during coition; posterior part of body round; suckers two, the anterior apical, surrounding the mouth; the posterior in close proximity to it, serving as organ of fixation. Central nervous system represented by a supra-œsophageal mass, concave on the ventral surface, and connected by fine filaments with minute peripheral nerve-masses distributed here and there in parenchyma. Excretory system composed of two parallel longitudinal canals, which anastomose posteriorly to open by an excretory pore. Reproductive system consists of five seminal glands connected with a seminal vesicle, the duct from which opens at bottom of gynæcophoric canal near its anterior end. The *female* is darker, more cylindrical, much finer, resembling a fine silk thread; attains a length of 20 mm., its fineness making it look considerably longer than the male; smooth and devoid of tubercles; anterior extremity much attenuated. Arrangement of digestive tract differs from that of male, the canals being very much larger, and having but one instead of several anastomoses. Reproductive system: the oviducts and the ducts of the yolk gland open close together into a simple gland from which leads the long combined utero-vaginal passage. The ova are generally arranged in a single or double row along the oviduct, with their spines directed backwards so as not to catch in passage.

The distribution of Bilharzia is Æthiopic. It is extremely abundant in Egypt. French soldiers are numerously affected in parts of Algeria, especially the hinterland. It is known at Axim, Accra, and other places on the West Coast, and also between Zanzibar and the Zambesi on the other side of the continent. From the Nyassa and inland Usambara districts it has been recorded. In Cape Colony it seems confined to the eastern provinces, and there, in certain districts of Natal, and beyond the Magaliesberg in the Transvaal, it is very common. It may thus be said to be discontinuously distributed over the entire continent. Other known localities are the Sinaitic Peninsula and Arabia; and though the Atlantic Islands are exempt from the scourge, Madagascar, Mauritius, and Réunion are said not to be. It has been reported from Sicily and from India, but further evidence is required, though there is nothing in the science of geographical distribution to forbid the possibility of its occurrence in these localities.

The symptoms are often sudden in onset, and generally first connected with the bladder, though sometimes a false dysentery may precede. They vary with the seat of invasion. If the posterior part of bladder be affected there is sometimes little pain. More commonly the neck of bladder and urethra are invaded, when there is often great pain in micturition, vesical tenesmus and irritation, and supra-pubic pain. Pain in the buttocks, the front of the thighs, and even in the legs is not infrequent; and if the prostate and vesiculæ seminales are attacked, perineal pain, priapism and seminal emissions often occur. Other seats of pain, of varying severity, are the inguinal and hypogastric regions and the lower part of the back; though these are more characteristic of a further advanced stage of the disorder. After an uncertain period there may be a remission of vesical and urethral pain and irritation owing to the parts having become, as it were, tolerant of the invader. General cystitis seems rarely if ever set up. Hæmaturia does not usually occur at first.

Sometimes the bowel shows the first signs of the disorder, the symptoms produced being not unlike those of subacute dysentery, with similar tormina, and the passage of blood and mucus with scybala. In other cases diarrhœa occurs.

The earlier symptoms are thus confined to the bowel or bladder, or both; and though often severe, are of a simple and primary type. Later, grave secondary mischief may be set up at these first seats of attack, or other organs may become affected. The ova of the parasite and the detritus in the bladder may become the nuclei of urinary calculus, and new growths form in the bladder or large intestine; occlusion of the ureter may occur and hydro-nephrosis supervene. Pyelitis or pyelo-nephritis, hepatic abscess, localised peritonitis, and even perforation of the bladder have been recorded. The symptoms of these various disorders may therefore be met with, but are not necessarily to be expected. Hæmaturia is nearly certain to occur not long after the onset of the disease. It is seen almost always at the end of micturition only, when about a teaspoonful of bloody urine is voided, pure blood rarely if ever; though blood-clots large enough to obstruct the flow are sometimes passed. An instance has been recorded of bleeding so copious that the urine formed a solid clot; but ordinarily the hæmaturia is not great. It is, however, tolerably persistent, often occurring daily or with but slight intermissions for months, or even years; it is generally increased by exercise, and especially by riding. The invasion of fresh areas of the bladder may produce a fresh train of symptoms similar to those at the onset of the disorder, with a recurrence of hæmaturia. It is noteworthy that the shirts of Bilharzia patients are almost always stained with blood. Of the steady drain on the system caused by the loss of blood anæmia is usually a marked symptom, and loss of flesh and strength attend it. Fibrillar muscular twitchings are occasionally troublesome, and severe epistaxis from the anæmia is sometimes met with.

The urine at the onset of the disease may present few deviations from the normal save the presence of minute specks, not so large as a pin's head, of a brilliant scarlet colour. Microscopically, the ova are probably to be detected, with a few pus cells and blood corpuscles (Fig. 65). As the case advances the detritus gradually increases, and the urine usually exhibits the following characteristics:—Quantity not altered, unless when organic affection of the kidney has supervened; colour usually darker than normal, often smoky, sometimes bloody; odour sweetish, peculiar, sometimes ammoniacal; reaction only faintly acid, or perhaps alkaline; clearness variable, the turbidity being nearly always well marked, and in some cases very great, especially in the morning. Though largely due to pus, mucus, or blood-cells, this turbidity is in part caused by the characteristic products of the platyhelminth. These, which to an experienced observer are quite pathognomonic of the disease, need more detailed consideration.

Detritus of the Bilharzia.—For convenience of description they may be divided into four classes:—1. Floating in the urine glass—for they take some time to settle—are seen colourless filaments, resembling threads of the finest white silk, usually unbranched, attaining a length of from 1 to 3 inches, and often showing in their substance minute specks of an opaque white or yellow colour. 2. Small, opaque, roundish masses, the largest not exceeding the head of a carpet pin in size, either white, yellowish, or bright red. 3. Particles almost exactly resembling small fragments of veins, deeply blood-stained, often with two or three branches, of all sizes up to $\frac{3}{4}$ inch in length and $\frac{1}{50}$ to $\frac{1}{10}$ inch in breadth, cylindrical in shape, but occasionally with slight fusiform dilatations. 4. Flattish blood-clots, which may attain the size of a shilling. The three last named usually sink at once to the bottom of the glass.

Under the microscope various objects are to be found: crystals of uric acid, or oxalate of lime, or the ammonio-magnesian phosphates, and an abundant organic deposit composed of pus and blood corpuscles, epithelial cells of nearly every size and shape, pigmentary particles, amorphous granules, and other débris. The long whitish filaments and the vein-like substances just alluded to are seen under a high power to consist of homogeneous fibres and mucous cells, forming a stroma in which are entangled and embedded the organic and inorganic objects above mentioned. Finally, great numbers of ova of the Bilharzia are usually to be seen; some free, others aggregated in masses, others included within the substance of the peculiar casts. Embryos are rarely or never to be found, as the ova cannot hatch in undiluted urine. The number of ova passed daily must often reach a total of thousands. It is said that many more are passed in summer than in winter.

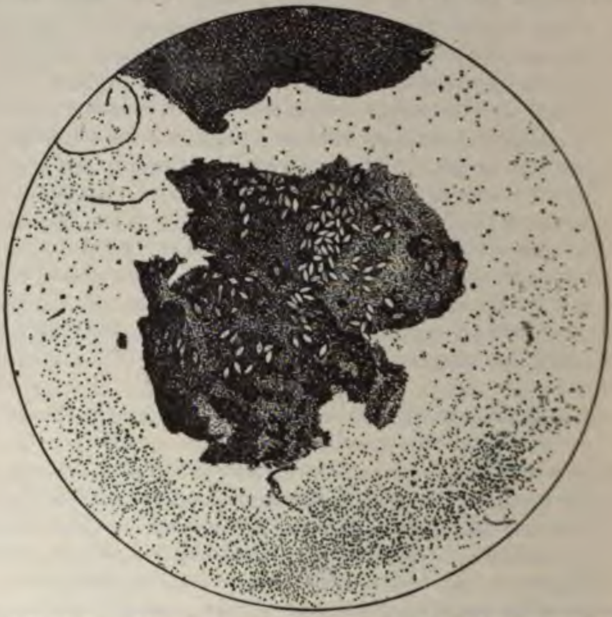

FIG. 65.—Fibrinous clot from urine showing ova of Bilharzia; slightly magnified. After Lortet and Vialleton.

Ovum and Contained Embryo.—The ovum (Fig. 66), which in appearance closely resembles a melon seed, is a bright, translucent, flattened, oval body, with a very sharply-cut outline, blunt at one end, but provided at the other with a small but acutely pointed spine. Sometimes, from reasons as yet unexplained, ova with lateral spines are found. The average length of the egg is from $\frac{1}{200}$ to $\frac{1}{160}$ inch, its breadth about half this. The egg-case, in spite of its hardness, is perfectly transparent, and permits the embryo within it to be clearly seen. The creature lies most frequently with its head towards the spine-bearing end, but the reverse position is also very common especially in Egyptian cases. The fact that in almost all cases the embryo is nearly ripe for extrusion renders it probable that the earlier stages of development take place within the body of the female. It is enclosed in a fine hyaline sac, but does not lie free within the ovum, being attached at what may be termed the shoulder; while between it and the shell are seen a number of highly refractive globules. The cilia covering the body, the body substance itself with its

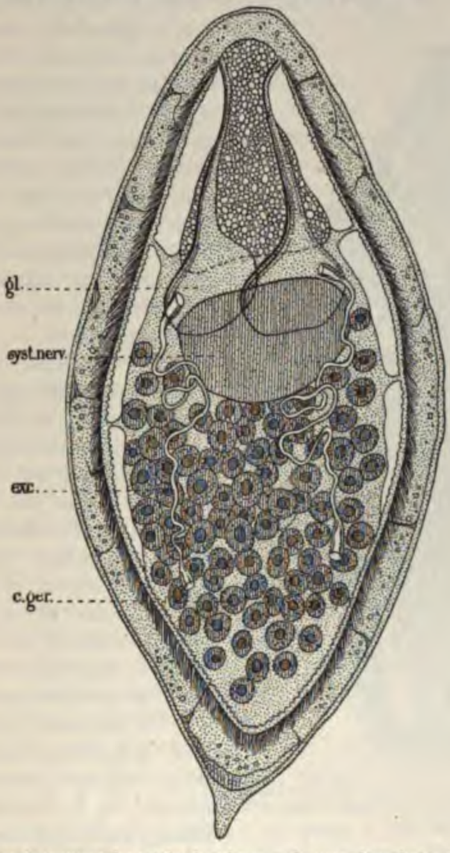

FIG. 66.—Bilharzia ovum and contained embryo. *gl.*, pear-shaped gland; *exc.*, excretory apparatus; *c.ger.*, germinal cells. After Lortet and Vialleton.

two pear-shaped organs towards the cephalic end, and the curious snout-like proboscis are all visible, and in the fully mature ovum slight movements may be noticed in the embryo.

The ova will soon hatch in pure water, even if it be quite cold; but if it be of a temperature of about 80° F. and the ova perfectly ripe, hatching takes place in the course of two or three minutes or even less. When they are less ripe the embryo appears to mature quicker than the tough shell; and the violent efforts made by it to burst its shell form one of the most curious sights of microscopy, the creature's movements and revolutions within the shell being so rapid that the eye can scarcely follow them. Suddenly the egg-case bursts with a longitudinal fracture, and the embryo darts with great rapidity out of the field of the microscope.

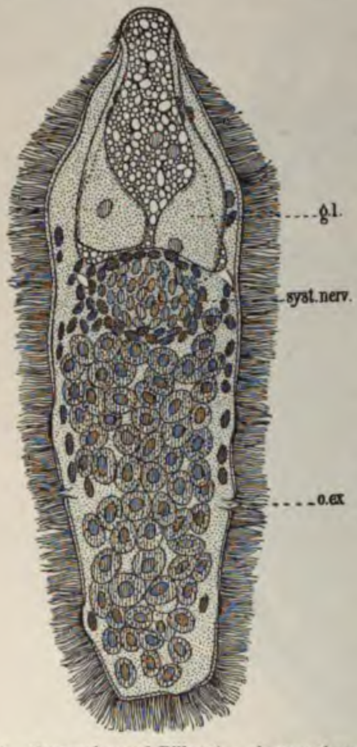

Fig. 67.—Free embryo of Bilharzia. *gl.*, pear-shaped gland; *o.ex.*, orifice of excretory apparatus. After Lortet and Vialleton.

Free Embryo.—The embryo while within the egg is ovoid; but directly it is hatched it assumes a more elongated shape, its broadest part being at the junction of the first with the second fourth (Fig. 67). The shape is, however, subject to great variation due to the contraction or elongation of the muscular fibres of the body. The ceaselessly moving oral proboscis is capable of protrusion and retraction to a considerable extent, and is the only portion of the body not clothed with cilia. The body-wall is composed of longitudinal and transverse muscular fibres, and the internal organs consist of a stomachal tube and two pear-shaped glands with tortuous canals—the primitive forms of a digestive canal, in short—besides a nervous and water-vascular system, and large germinal cells which occupy a great part of the posterior half of the body, and are probably destined to form the next generation of sporocysts (*rediæ*). The animal swims with great speed by the motion of its cilia. Its duration of life in this stage is uncertain. Cobbold, Lortet, and others have never been able to keep it alive more than a day, but I have found some alive on the fifth day after hatching. Water at all impure, or containing decomposing animal matter, soon kills them.

Life-history.—The most careful research has, up to the present, failed to reveal the complete series of metamorphoses which Bilharzia undergoes, and of the hosts in whose bodies these changes are effected. The life-history of the closely allied liver-fluke is as follows:—The ova, passed in the sheep's droppings, are washed into ponds or ditches by rain. There the embryo hatches, and immediately penetrating the body of the snail *Limnæa truncatula*, forms a sporocyst containing *rediæ*, within which are developed the armed *cercariæ*, tailed larvæ resembling tadpoles, which pass out of the snail and fix themselves on blades of grass, etc.; there they are eaten by the sheep, and the life-cycle is thus completed. The probability therefore is that Bilharzia goes through similar metamorphoses; and this is strengthened by the fact that all attempts to infect monkeys and other animals by prolonged feeding on living embryos have been in vain. That the embryos have in no case been found to invade the bodies of the fish, reptiles, or molluscs, which experimenters have placed in tanks with them, merely proves that the right host has not yet been discovered.[1] Sonsino's theory of "auto-infection"—in other words, that the animal once lodged in its human host is capable of completing its life-cycle therein—may be confidently rejected, not only on account of its zoological improbability, but from the fact that the embryo will neither hatch nor live in urine or blood.

The mode of infection is thus unknown. It is not even certain that it occurs by the ingestion of the animal; many competent authorities believe that the armed embryos directly penetrate the skin, urethra, or anus during bathing. In no other way is it easy to account for the absence of the disease in infants and young children, and for the very remarkable fact that among European females it is extraordinarily rare. Thus Brock in South Africa, among many hundreds of cases, never saw a female affected. River-bathing is very seldom indulged in by women in South Africa, but the male youth are much in the water. Among natives the women are apparently more frequent sufferers, but they have often to ford streams, and may daily be seen wading up to their knees to fill their jars and calabashes for household use.

The period of incubation may be as little as four months. Old soldiers have been known to make no complaint until many years after they have returned from an infected locality, but it is hardly credible that no symptoms occurred during so long a period. Many of the plantation coolies in Natal show the affection within six months of their arrival in that colony. Although old and young are equally vulnerable, the disease in South Africa is most frequently seen in boys under the age of puberty.

Diagnosis.—Microscopic examination of the urine, or even its naked-eye appearance to the person familiar with the disease, should at once remove all doubt concerning the case. By careless or ignorant practitioners the malady is sometimes regarded as cystitis, Bright's disease, or calculus; and if the latter be really present the origin of it is doubtless often overlooked.

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[1] It is worthy of remark that *Melania tuberculata*, Müll., seems never to have been tried, yet its geographical distribution appears to be identical with that of Bilharzia, and as a tolerably abundant fresh-water mollusc it offers favourable conditions.

Pathology.—Bilharzia is found in various parts of the human body, but its focus appears to be the smaller branches of the portal vein, where large numbers (over 300) have been counted. The males greatly preponderate; indeed, in most autopsies no females are found. Such of the latter as are discovered are generally in sexual combination. It seems probable that after impregnation the female moves into the smallest vessels she is able to attain, and there deposits her eggs (Fig. 68). The intimate relation between the chylopoietic veins and the systemic veins supplying the genito-urinary passages accounts for the special affection of the bladder, rectum, kidneys, and ureters. Ova may be found, however, in many organs and parts, even in the lungs and skin, and in the left ventricle of the heart; but, according to Lortet and Vialleton, never in the spleen, the pancreas, or the stomach. The liver, curious to relate, is seldom pathologically affected.

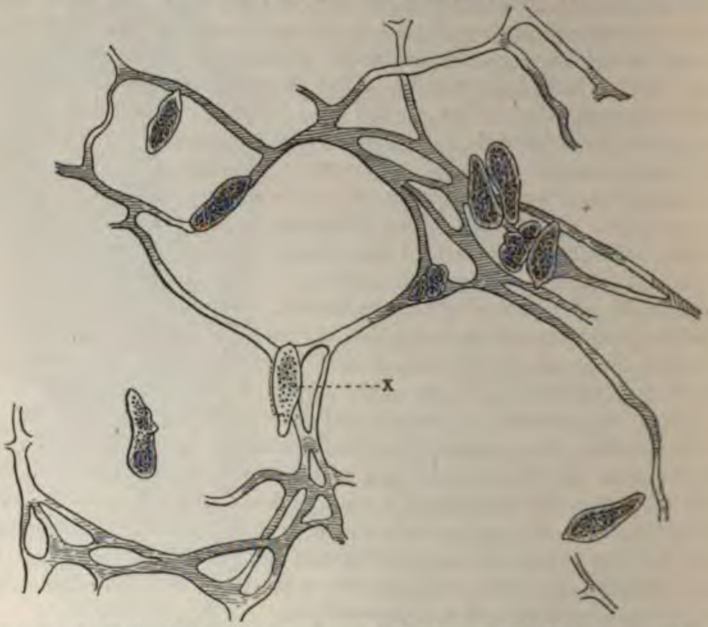

FIG. 68.—Capillaries of the vesical mucous surface, highly magnified, showing ova within, and, at X, partly escaped from the vessels. After Lortet and Vialleton.

The harm is wrought, not by the animal itself, but by its ova. Laid by the female in countless thousands they block the vessels, cause blood stasis with exudation, and subsequently chronic local inflammation. The long-continued irritation gives rise to new growths; hence we find fibro-adenomas of the large bowel, epitheliomas of the bladder, etc. In the latter viscus the usual naked-eye appearances are patchy induration and

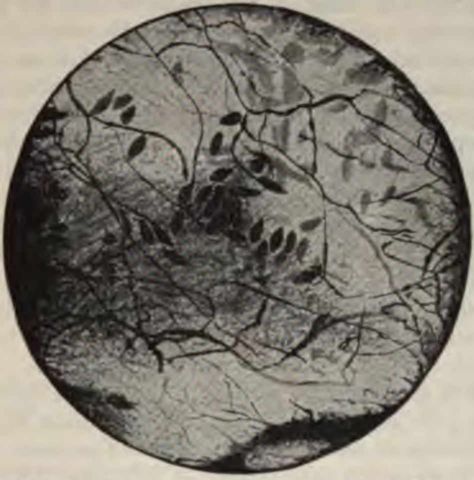

FIG. 69.—Surface of mucous membrane of bladder from a case of Bilharzia disease. After Lortet and Vialleton.

injection of the mucosa, the affected part being encrusted with urinary deposits, or perhaps covered with ragged ulcerations (Figs. 69 and 70). The

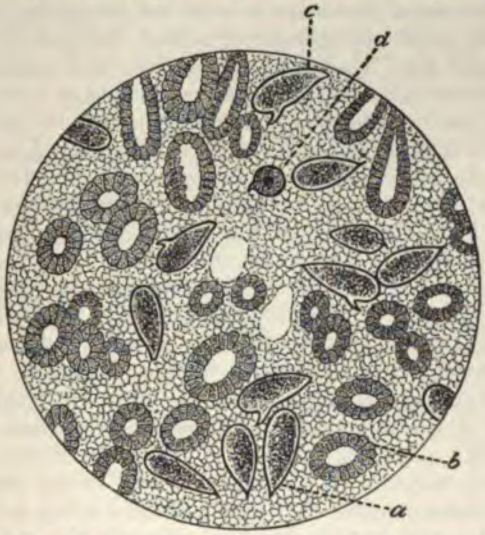

FIG. 70.—Section from rectal mucous membrane from a case of Bilharzia disease. *a*, normal ovum; *b*, section of a follicle; *c*, ovum with lateral spine; *d*, laterally spined ovum seen in transverse section. After Sonsino.

ova are generally situated in the mucous or submucous layers, and the bladder walls are much thickened, partly from hypertrophy of the muscular coat, partly from an interstitial growth of fibrous tissue. If the kidney and ureters be affected, like changes are set up. An interstitial nephritis may occur, and the gradual thickening of the walls of the ureters may lead to complete occlusion and consequently to pyo- or hydro-nephrosis. In the lungs the ova do not appear to give rise to much specific mischief, though they probably render the patient more liable to pneumonia and tubercle. The pathology of the curious vein-like and thread-like substances usually found in the urine is uncertain. Dr. John Harley (37) considers that "the mucus in which the ova are embedded is derived from the crypts in which the animal takes up its abode, the growth of mucus corpuscles being due to the irritation of the parasite and its eggs. As the mucus fills the crypt it is forced out by the continual production of the ova, and is thus roughly moulded . . . in the form of strings."

The prognosis will depend not a little upon the amount of the infection, and will thus be more serious in the case of an Egyptian fellah long resident in a Bilharzia-infested district than in an European who has acquired the disorder in the course of travel. The cases seen in Egypt are apparently more severe than those in Southern Africa, probably on this account, and in the latter country death rarely ensues as a direct result. In a large number of cases where boys from six to fifteen years of age are affected, the disease is apparently cured at puberty, though an examination of the urine may reveal ova for some years afterwards. The prognosis in the case of adults is no doubt less favourable than in that of boys, and on the whole the probability is that the patient will never be a perfectly sound man again; though he may live many years, and be capable of moderately hard work, he may be liable at any moment to an exacerbation of the disorder. The axiom that "the life of most entozoa corresponds with that of their host," must be remembered, and no assurance of the certainty of the creature's disappearance be given. A case is known to the writer in which the patient suffered from a severe attack eighteen years from the onset of the disorder, which had been in abeyance for some years. The presence of secondary complications, such as stone or renal mischief, will of course greatly increase the gravity of a case. A consideration of the proportion of the population affected in various localities shows that the disease is not in all cases so lethal as some physicians describe. In parts of the Transvaal "a very large proportion of the male population" suffers from it; "the complaint is referred to as if the appearance of blood in the urine of boys were little more than a physiological fact" (Brock). In Pietermaritzburg "it seems as if the majority of the male youth" were affected (Batho). Lortet and Vialleton consider that from one-third to one-half of the native population suffer, and another observer estimates the proportion among the dwellers by the Sweet-water Canal as not less than fifty per cent.

Treatment.—The chief aim will be to sustain the patient's strength and to combat symptoms. When it is considered that the chief seat of the parasite is in the portal vein, the utter uselessness of medicated injections of the bladder, recommended by some physicians, needs no demonstration. They have, moreover, in some cases proved extremely harmful. Dr. Fouquet of Cairo claims to have had success with the etherial extract of male fern, which perhaps might be tried, but until some diffusible anthelmintic be discovered powerful enough to destroy hæmatozoa without injuring the host, little can be done. Free diluents may be used with advantage, a non-stimulating diet recommended, and a watch kept for symptoms of calculus. With regard to prophylaxis, all drinking-water should be boiled, fresh-water bathing eschewed, and the eating of watercress and fresh-water fish avoided.

F. H. H. GUILLEMARD.

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F. H. H. G.

HYDATID DISEASE

Historical.—The history of the growth of our knowledge concerning hydatids, as understood in this article, is intimately associated with that of bladder-worms in general; especially in all that relates to their biological aspects.

There is little doubt that as a pathological phenomenon hydatids were recognised by Hippocrates. He writes: "When the liver is filled with water and bursts into the epiploon, in this case the belly is filled with water and the patient dies" (6). Aretæus still more specifically indicates the disease as a form of dropsy due to "small and numerous bladders full of fluid," and he goes on to speak of the blocking of the canula by the bladders in paracentesis. They are again mentioned by Galen in his comments on the above-quoted aphorism of Hippocrates, which, in his opinion, refers to hydatids.

Evident allusions to hydatids and other bladder-worms occur in the works of the medical writers of the sixteenth and seventeenth centuries without, however, any recognition of their animal nature. The term, moreover, is frequently applied to encysted accumulations of watery fluid of many kinds.

It was not until 1684 that the animal nature of bladder-worms appears to have suggested itself to Redi; and in 1685 and 1691 respectively Hartmann and Tyson reached similar conclusions apparently independently of one another.

Pallas studied the subject of bladder-worms between 1760 and 1767, and clearly recognised a relationship with tænia. According to him all bladder-worms were forms of tapeworms, to which he gave the name *Tænia hydatigena*. He also recognised that the livers of sheep and cattle contained bladders having characters different from those of other vesicular worms; and he drew important distinctions between adherent serous cysts and non-adherent hydatids, remarking that "it is probable that the latter sometimes observed in the human body are either a species of vesicular tænia or of those *Hydatides singulares* that I have observed and described in the liver and lungs of sheep, which ought certainly to be ascribed to a living creature." He observed, without recognising their nature, the echinococcus heads in the *Hydatides singulares;* and, moreover, was the first to suggest the experimental administration of eggs of tænia to animals.

The observations of Pallas were confirmed by Goeze in 1782, who further indicated the existence of the general membrane lining the vesicles, and considered the echinococcus heads to be tæniæ.

More or less clearly expressed references to hydatids in the human subject occur towards the close of the eighteenth and beginning of the nineteenth centuries; and in 1821 such a case is specifically described by Bremser, and in the following year by Rendtorff.

Laennec, meanwhile, having failed to find in the hydatids of man the echinococcus heads with which he was familiar in the hydatids of domestic animals, nevertheless recognised their animal nature, and founded for them a separate genus which he called Acephalocystis.

So far the exact relationship of the bladder forms to the tænia head had not been made apparent; but a great impetus to our knowledge was given in 1842 by the application of Steenstrup's theory of the alternation of generations to the cystic worms. In the light of this discovery Dujardin, Von Siebold and Van Beneden investigated the subject without, however, fully appreciating the true characters and relationships of the bladder forms.

Our exact and systematic knowledge of this subject may be said to date from the feeding experiments of Küchenmeister in 1851. By this means the fact was clearly demonstrated that certain bladder-worms are the larval stages of certain tapeworms. In the following year, by the successful breeding, in the dog, of *Tænia echinococcus* from echinococcus cysts of the domestic animals, a similar relationship was proved to exist between these two forms by Von Siebold and, shortly afterwards, by Küchenmeister. These experiments were repeated by Haubner, Leuckart and Nettleship.

With human echinococci the experiment failed in the hands of Küchenmeister and Zenker, but a measure of success attended Naunyn in Berlin and Krabbe in Iceland. More recently similar successful experiments with human echinococcus cysts were carried out by Thomas in Adelaide, South Australia.

The converse experiment of administering the ova of *Tænia echinococcus* to animals was carried out by Leuckart in conjunction with Haubner in the case of the lamb, sheep and goat, without definite results, though it is probable that even in these experiments migration of the embryos into the viscera did take place; in the case of the pig, however, the experiments were eminently successful, and served as the basis of much of our knowledge concerning these parasites. R. Leuckart has exhaustively treated the whole subject of human parasites in his work *Die Parasiten des Menschen*, partially (1895) translated into English by Hoyle—a work which is essential to every student of helminthology.

Largely through the labours of the investigators whose names have been specially mentioned, as well as through those of Livois, Huxley, Wagener, Virchow, Rasmussen, Davaine, Cobbold, Busk and others, the views have been established which will guide us in describing the anatomy, systematic position, development, and life-history of these parasites.

Of the radical treatment of hydatids, to be advocated in this article, the credit belongs to Lindemann, who appears to have first operated in this way in 1871; though no account of the operation seems to have been published for some years subsequently. This procedure has of late been persistently advocated by various Australian surgeons, more particularly by those of Adelaide, South Australia, amongst whom may be mentioned Dr. Gardner and the late Dr. Thomas; it is now generally adopted throughout the hospitals of Australasia.[1]

Biology.—Many of the internal parasites which take up their abode in the body of man are due to involuntary importations of organisms from the domestic animals. Amongst these the dog is the immediate source of those generally known as hydatids. This term, sanctioned by long usage, is applied to the larval or bladder stage of *Tænia echinococcus*, one of several parasites which are found within the alimentary canal of the different varieties of the domestic dog and of one or two allied species.

There are other parasites which exhibit a bladder phase of existence, such as cysticercus and cœnurus; but general custom, in English-speaking countries at any rate, is inclined to restrict the term hydatid to the vesicular organism derived from the ovum of *Tænia echinococcus*, and it would be well that it should be exclusively so restricted. The name Echinococcus (ἐχῖνος, a hedgehog; κόκκος, a berry—introduced by Rudolphi in 1801), or Echinococcus disease, which is frequently used, especially by foreign writers, has undoubtedly the advantage of indicating the zoological relationship with the mature organism; but it is not always easy, and we think in this case not desirable, to dislodge a name that is not only well established and well understood, but also expressive of a chief physical characteristic. Moreover, the name Echinococcus is not always used in the same signification, being by some applied to the characteristic bladder itself inclusive of its contents, and by others restricted to those structures that will afterwards be described as scolices or echinococcus heads.

Description of the Adult Tapeworm, Tænia echinococcus, V. Siebold—Definition.—A tapeworm of comparatively small size (Fig. 71), and with only three or four joints, of which the last, when mature, exceeds all the rest of the body in size. The total length is but a few millimetres, at most five. The small hooks have stout root processes, and are seated on a somewhat swollen rostellum. Their number usually amounts to some thirty or forty (Leuckart).

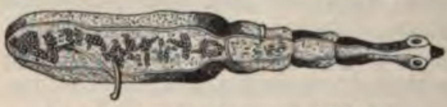

FIG. 71.—*Tænia echinococcus* (× about 11). From Leuckart.

To this definition we may add that the hooks, forming two series of from fourteen to twenty-five each, of which those of the inner row are the larger, are inserted into the base of the rostellum or proboscis-like anterior termination of the cephalic extremity, which in this species is somewhat pointed and prominent. By the musculature

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[1] See papers and discussions on "Hydatid Disease," *Transactions of Intercolonial Medical Congress of Australasia*, 2nd and 3rd sessions. For a very copious bibliography of all that relates to the biology of the Cestode worms see Rolleston's *Forms of Animal Life*, 2nd edition, edited by Jackson. The manual of Cobbold and the monograph of Neisser (13) also contain many bibliographical references to hydatid disease. Historical references are to be found in the treatises of Küchenmeister and Davaine.

of this region the hooks are moved. They are further characterised by the relatively large size of their roots, but they vary in this respect according to the age of the worm (Fig. 72). They are often found deficient in number. Behind the circlets of hooks are four suckers radially disposed; behind these the head elongates and narrows to form a neck. The next succeeding segment, or first proglottis, is imperfectly defined; it is short, and broader than the neck. The third segment, or second proglottis, is longer and broader than the preceding, and in it the reproductive organs can already be distinguished. The fourth or terminal segment shows a great increase in size, and contains, besides the completely developed reproductive organs (Fig. 73), fully formed and hard-shelled eggs to a number estimated at 500, in which can be recognised the hexacanth embryos.

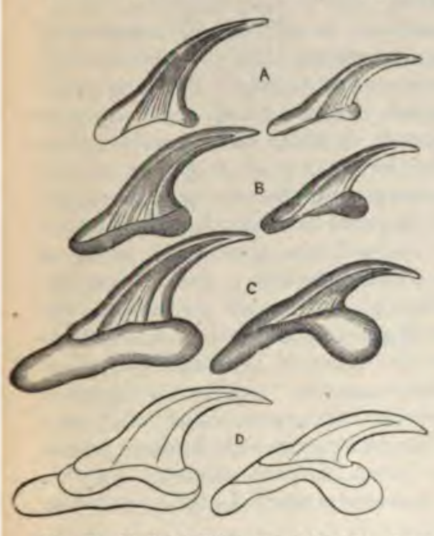

Fig. 72.—Hooks of Echinococcus (× 600). From Leuckart. A, *Echinococcus veterinorum*; B, *T. echinococcus*, third week; C, *T. echinococcus*, adult; D, the outlines of the three forms drawn one within the other to show their gradual changes.

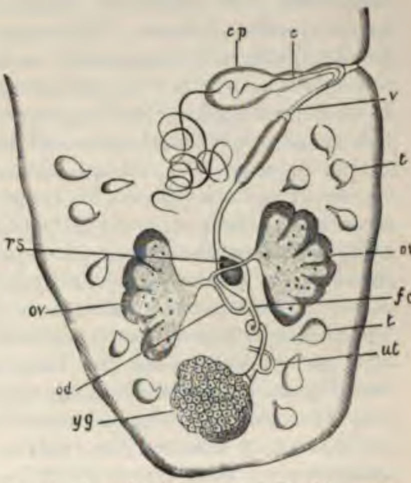

Fig. 73.—Reproductive organs of *T. echinococcus* during fertilisation (× 80). From Leuckart. *t t*, testes; *c.p.*, cirrhus pouch; c, penis; *ov.*, ovary; *od.*, oviduct; *r.s.*, receptaculum seminis; *y.g.*, yolk glands; *ut*, tube probably leading to uterus; *f.c.*, fertilising canal; *v*, vagina.

These worms are found, often in immense numbers, in the upper half of the small intestine of the dog, where they are apt to lie concealed amongst the villi. Under appropriate conditions they may be observed to exhibit active movements, in which the body may broaden or become extremely attenuated. Their duration of life cannot be stated with precision.

When the ripe terminal proglottides break off they are extruded with the fæces. Their soft tissues soon decay, and the liberated ova, enclosed and protected by their resistant chitinous envelopes, become scattered upon the soil or herbage, or get washed into collections of surface waters.

Under these conditions the embryos, or possibly, under certain circumstances, the entire proglottides, may find their way into the alimentary canal of those domestic animals which are capable of serving as hosts for the subsequent phases of development, or it may be into that of man himself.

If so ingested, the protecting chitinous envelope is dissolved or ruptured by the combined warmth and solvent action of the digestive fluids; and the embryo, thus set free, begins an active life, boring, or rather pushing its way, by means of the movements of the hooks, through the gastric or intestinal walls. No one, we believe, has actually found the embryos in process of traversing these organs, but they have been found by Leuckart in the portal vessels.

The route taken by these active embryos is still largely a matter of conjecture; the influences which may determine their distribution will be discussed elsewhere. From the frequency with which they are found in the liver, it is reasonable to suppose that the usual, or at any rate a frequent course is into the portal system, in which, as just stated, they have been found. Possibly, however, they may push their way among the actual or potential spaces of the connective tissue elements of the body; or, it may be, though there is no proof of this, that they travel in the lymphatic spaces or vessels. Indeed, the absence of proof of hydatids in the lymphatic glands and closed lymphatic vessels is remarkable, and must be taken into account when we seek to explain the distribution of the bladders by a mere passive migration; so likewise must the conspicuous preference for the brain of the allied organism cœnurus, which produces the disease known as the "gid" or "staggers"; that of cysticercus for the intermuscular connective tissue; and, to a less degree, that of the echinococcus for the viscera—preferences which may be taken to indicate something like a selective affinity. Be this as it may, whatever the route or however impelled, the wandering embryo eventually comes to rest.

Growth of the resting embryo or proscolex—Development of the Echinococcus bladder.—At the earliest stages at which these resting embryos have been with certainty observed—namely, by Leuckart in the pig four weeks after feeding with ripe proglottides—they form solid spherical bodies measuring 0·25 to 0·35 mm. in diameter, and bear a striking resemblance to a mammalian egg; that is to say, a thick, homogeneous, transparent and elastic cuticle or capsule (ectocyst, Huxley) encloses coarsely granular contents, as the zona pellucida encloses the granules of the yolk. In the course of subsequent development the proscolex increases in size, the external envelope becomes indistinctly laminated, and the contents more transparent, owing to a partial liquefaction. Fluid has, in fact, begun to accumulate in the interior, and the solid mass has become a vesicle with a gradually increasing quantity of fluid. With comparatively slight increase in the size of the vesicle an internal lining membrane appears upon the inner surface of the cuticle. This constitutes the germinal or parenchymatous layer (endocyst, Huxley).

In it can be recognised granules and cellular structures of which some are pale and drop-like, others granular or exhibiting radiate branchings. The lamination of the cuticle becomes more marked, and remains always a conspicuous and characteristic feature; its thickness increases with age. Meanwhile, even at this early stage, the presence of the growing organism, like other foreign bodies, excites changes in the tissues which harbour it; thus, by processes which will be discussed hereafter, an enveloping capsule of connective tissue is formed, bounding the parasite externally: this has been said to be lined internally by cellular elements, and is the fibrous sac or adventitious capsule.

This structure, often improperly called ectocyst, though it is in no sense an organic part of the parasite, is nevertheless important to it as the immediate source of its nutritive supply. Davaine and other authors with good morphological reasons maintain that the name cyst should be applied to this structure alone; but this name, by most writers, has been attached to the bladder-like organism itself; so that it is more convenient to retain this signification.

In the parasite itself a vascular system has not hitherto been recognised beyond doubt; moreover, the musculature which confers mobility upon some other larval forms is scanty. No trace of sexual organs exists. Amongst the cells of the parenchymatous layer are lenticular, laminated, calcareous particles, chiefly composed of carbonate of lime, which resemble in many respects corresponding bodies which form constant and characteristic elements in the cortical region of the body parenchyma in the mature tapeworm, and indeed in the cestodes generally. Compared with other forms in the bladder stage, that of *Tænia echinococcus* undergoes relatively slow growth; but, even when no more than 15 to 20 mm. in diameter (Leuckart), or, sometimes in our experience, considerably less, an important development may be already in progress which still further distinguishes this proscolex from other varieties of bladder-worms: this is the formation of numerous heads or scolices.

The vesicular or bladder stage of tænia may (*a*) give rise to a single head; the resulting organism is then a cysticercus; (*b*) it may produce many heads, and the resulting organisms are termed cœnurus; or (*c*) there may be, as in echinococcus, many heads; these, however, are not produced directly from the germinal layer, as in the previous instances, but indirectly from special delicate sacs called brood capsules,[1] which themselves originate from the proscolex or bladder-worm.

Development of brood capsules and scolices (Figs. 74, 75).—These structures arise as minute elevations in certain parts of the germinal layer by proliferation of its cells, which, according to Naunyn, bear vibratile cilia that may persist even on the matured capsule. Within these elevations a small spheroidal cavity makes its appearance, gradually increases in size, and becomes lined internally with a delicate cuticular membrane; externally is a layer of cellular structures. The wall of the brood capsule thus exhibits two distinct layers, comparable to those of the mother bladder but inverted in relative position, which suggests that the brood capsule represents an invagination of the former. Process and cavity grow to three or four times their original diameter, and, when fully grown, may attain the size of millet seed or about 1·5 mm. in diameter. Though muscular fibres have not been found in them, the brood capsules exhibit active movements. They are extremely delicate and fragile, and thus it happens that unless special care be taken in the examination, or if the material be stale, they become ruptured, or may even escape observation altogether. This has led to the view that the connection between the heads and brood capsules is only temporary, and that after separation the living scolices may float free in the fluid of the mother bladder. Leuckart, however, insists that all parts of the echinococcus—mother bladder, brood capsules and heads—are throughout life in direct continuity with each other.

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[1] This statement, implying that the scolices are invariably derived from brood capsules, though generally accepted, probably goes too far and may have to be reconsidered. We have recently had the opportunity of examining a specimen which shows four heads sprouting directly from the germinal membrane of an exogenously developed daughter cyst (human), of a size less than 1 mm. in diameter—smaller, in fact, than a brood capsule—and possessing a relatively thick cuticula. Leuckart refers to similar observations (10).

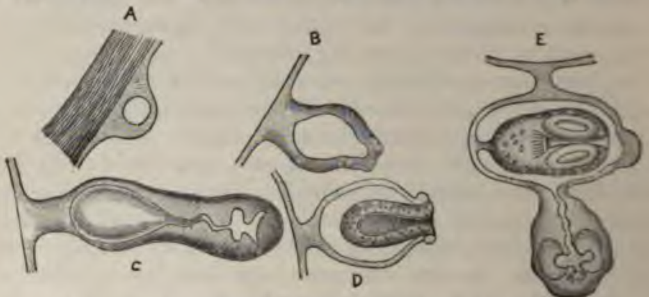

Fig. 74.—Early stages of development of brood capsule and scolices.

A head (scolex) first appears as a discoidal thickening in the wall of the brood capsule, which, relatively to the latter, grows into an externally situated club-shaped process perforated longitudinally by a canal-like continuation of the interior cavity of the brood capsule. Though thus appearing as an external protrusion of the brood capsule, it may at times be temporarily inverted, and indeed is frequently found so. At the bottom of the distal end of this hollow protrusion—namely, at that which is farthest from the point of its attachment—the distinctive elements of the scolex—the suckers and hooks—are formed, the latter first appearing as a thick fringe of prickles which subsequently all disappears except the foremost rows.

Histological differentiation progresses, and muscle fibres, vessels and calcareous particles become evident. At this stage the head as a whole becomes permanently inverted into the cavity of the brood capsule; the contiguous walls of the hollow bud, and of the still hollow stalk by which it is attached, fuse; the scolex thus becomes a solid body attached to the interior of the brood capsule by a slender muscular stalk. The anterior portion of the head which bears the suckers and hooks may, however, be invaginated within the remainder or hinder part, and may remain so for some time.

The views here adopted of the growth of the heads, often given in his own words, are those of Leuckart, who insists on the points that the scolices originate normally from the exterior of the brood capsules and as hollow buds, in contradistinction to the views of other writers, who maintain that they arise from the interior or as solid bodies.

In this way, by successive development, heads of different ages to the number of ten, fifteen, or twenty may come to lie within one capsule. In the case of large bladders the included capsules may increase to the number of many thousands.

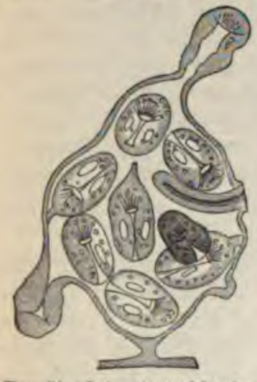

FIG 75.—Later stage of development of brood capsule showing external and internal scolices.

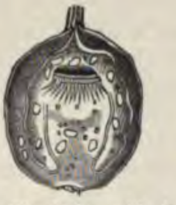

FIG. 76.—Scolex with invaginated anterior extremity.

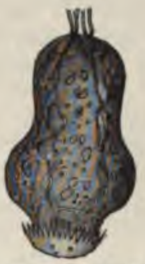

FIG. 77.—Scolex partially constricted.

The young scolex, in the stage which it has now reached, has a spheroidal shape of about 0·18 mm. in diameter. As Leuckart remarks, it bears a striking resemblance to a vorticella with its ciliary circlet retracted; and, as several heads are frequently seen in a group attached by their slender peduncles to a portion of the collapsed or ruptured brood capsule, the further resemblance to a colony of these animals is equally remarkable. In the depression left by the invagination of the anterior extremity within the rest of the head are the suckers and the rings of hooklets, which can be seen shining through its translucent tissue (Fig. 76); under certain conditions—that is, by gentle warming of the natural fluid of the bladder—the heads may be made to exhibit movements, evaginate the retracted portion, and assume an extended form with a length of 0·3 mm. In this state they have the shape represented by Fig. 76, in which a partial constriction divides the head into an anterior and a posterior part. A small pit at the hinder end, which receives the attachment of the stalk, remains visible for some time after separation from the latter.

The hooklets have a general resemblance in form and arrangements to those of the head of the adult worm, differing only in the shorter and more slender shape of the roots (Fig. 72). In fact the description of the head of the adult worm may stand for that of the scolex in the stage of development which it has now reached. On reaching the intestine of the dog, or other suitable host, the proglottides of the strobila or sexual worm are successively formed by a process of lengthening of its posterior end accompanied by transverse segmentation. The whole course of development, from the scolex condition to that of the adult worm, probably occupies a period varying from four to eight weeks.

Formation of daughter bladders. — The hydatid bladder, as we have traced it, consists of a single simple sac or mono-cyst, which may, however, attain an enormous size, bearing on its interior surface brood capsules which contain scolices in varying number and stages of development. From the fact that this kind is common in the domestic herbivora it has received the name of *Echinococcus veterinorum*; but, in our experience, it is frequently found in man. There may, however, be a greater degree of complexity in its structure in which secondary and completely separated bladders may be formed; and these may either lie inside or outside the primary or mother cyst.

The former, or endogenous type, that usually occurring in man (*Echinococcus endogenus*, Kuhn; *Echinococcus altricipariens*, Küchenmeister; *Echinococcus hydatidosus*, Leuckart), may arise by a vesicular transformation of the scolices, by a similar process affecting the brood capsules, or by infoldings of the parenchymal layer. In any case separate secondary or daughter bladders are formed which lie within the parent cyst, and they correspond to them in structure and behaviour, and may likewise give rise to brood capsules and scolices. By a resumption of the metamorphoses which have been described, the daughter bladders themselves may bud endogenously or exogenously, and thus produce a third or even a fourth generation within or without themselves; the whole brood being contained within the mother bladder.

The exogenous type, also occurring frequently, like the simple bladder, in the domestic animals and especially in the pig, is less common in man. It constitutes the form most appropriately named *Echinococcus exogenus* (Kuhn); but it has also been termed *Echinococcus simplex*, *Echinococcus granulosus* (Leuckart), *Echinococcus scolicipariens* (Küchenmeister).[1]

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[1] It would have been more appropriate and certainly less confusing if the term *Echinococcus simplex* had been restricted to the really simple or single bladders, while the name *Echinococcus veterinorum* might have been retained with some, though less, propriety as a synonym for the exogenous form. Indeed, in conformity with our views as to the specific unity of all the varieties of echinococcus bladder-worms (which are here adopted without argument), it would be well if the various Latin synonyms were abolished altogether from our nomenclature. We should then speak clearly of the simple, exogenous, endogenous, multilocular, or other varieties of echinococcus cysts.

In this form the secondary bladders arise from small granular masses which appear in the deeper layers of the cuticle of the mother cyst, though probably they are actually derived from the parenchymal layer. These assume a special cuticular covering of their own, and their central parts clear up and liquefy. With the continued centripetal formation of new layers in the cuticle of the mother bladder, and the rupture of its outer layers, these new formations gradually make their way externally, as completely separated sacs undergoing their subsequent development outside of the mother bladder, and usually close to it. In some cases, however, as in hydatids of bone (on the theory of their exogenous development), the individuals of the resulting broods may lie at a considerable distance from one another and from their common parent.

A peculiar and rare variety referable to the exogenous type has received the name of *Echinococcus multilocularis* (Virchow). Usually of comparatively small size, though it may grow as large as a child's head, it has hitherto been found most frequently in man, and for a long time was known only in the liver. Until Virchow demonstrated its true nature by the discovery in it of echinococcus remains, its peculiar appearances led it to be regarded as a kind of alveolar colloid cancer. More recently investigations by the same author incline him to believe that the bones must also be considered as a nidus in which hydatids may assume the same alveolar or multilocular features; these features, in his opinion, are due to the special characters and conditions of the organ in which the parasites occur. In the liver the hydatids of this variety may be so disseminated here and there in the substance of the viscus as to form a principal mass with other more or less voluminous cystic groups about it; or, otherwise, the whole tumour may be single and rounded. Section of it shows a thick fibrous capsule and an internal stroma, which forms by its meshes a number of loculi or alveolar cavities of small though varying dimensions. In these loculi are gelatinous masses, which are degenerating hydatid vesicles; each loculus is occupied by at least one of these vesicles, the larger containing several. This variety has, moreover, a tendency to a kind of central ulceration resulting in the formation of large anfractuous cavities filled with exudation products, decomposing material, and, in the liver, biliary products. The precise manner of growth and development of this special form is yet uncertain; but Virchow has shown (2) that as soon as these multilocular hydatids of bone extend beyond its confines into the surrounding soft parts, they may assume the habit of the ordinary exogenous (and also in our experience that of the endogenous) kind, and form large bladders; which supports the view that they are merely a variety of the type, and that their special conformation is determined by the physical and physiological characters of the nidus and not, as was at first believed, by a specific difference in the organism. A gelatiniform degeneration of the bladders is a usual feature in spontaneously retrogressing hydatids, and the existence of loculi is in itself of common occurrence in other forms. Every degree of sacculation, indeed, may exist, from a mere bulging of the wall, or simple constriction, to a state in which there are numerous intercommunicating cavities, the whole being surrounded by a common adventitia adapted to the various loculi.

Sterile hydatids.—Some hydatids contain no scolices, and the absence of scolices is frequently associated with the absence of daughter bladders — they are in fact sterile, and constitute the structures described as acephalocysts by Laennec. We cannot enter into a discussion of the manifold causes of this sterility, the frequency of which may easily be exaggerated on failure to find the evidences of reproduction. Juvenility, senility, inherited debility and degenerations in the parasite itself are conditions which, as in other organisms, may play their part; but probably the supply of nutriment is the chief, the vascular and other conditions of the adventitious sac or of the surrounding tissues being important factors. Thus certain pedunculated hydatids of the peritoneum, which are attached to the mesentery by extremely long and attenuated pedicles, have been found sterile or nearly so. On the other hand, if the production of daughter cysts be taken as evidence of fertility, it is remarkable that in the case of a hydatid bladder found lying free and naked in the peritoneal cavity these structures existed in abundance. Again, hydatids in the brain are said to be more frequently sterile than in other parts; a fact which may be related to the occasional absence of the adventitious sac, or to a tenuity of it so extreme that it is unrecognisable as a separate structure.[1]

Conditions determining the prevalence of hydatid disease.—The parts played by the dog on the one hand, and by man and the domestic ungulates on the other, have been more precisely indicated in the paragraphs relating to the life-history of the parasite. The intervention of animals so closely associated with the domestic and economic life of man, as essential factors in the genesis of a serious human disease, thus becomes a matter of prime importance. It is necessary, therefore, to examine more closely the experimental and other evidence which has not only led us to connect the prevalence of the disease in man with the dog and the domestic animals, but has also furnished us with precise biological results.

So far as is known, the adult *Tænia echinococcus* has only been found in the domestic dog, the wolf and the jackal. We do not know that it has ever been found in the Australian wild dog (*Canis dingo*); the dingo, however, may be a factor of some importance in the prevalence of hydatid disease in the outlying districts of the Australian colonies. The assertion of an eminent helminthologist that man himself may be the host of this tapeworm remains unsupported.

As the wolf and the jackal are not, as a rule, brought into relation with man,[1] the domestic dog remains as the chief host of the sexual worm.

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[1] Scolices or hooklets were observed in eighteen out of ninety-seven cases of hydatids of the brain (16).

On the other hand, the bladder stage of the parasite is much more widely distributed; it has been found in man, the monkey, lemur, sheep, ox, pig, deer, camel, giraffe, horse, ass, zebra, kangaroo, squirrel, seal,[2] cat; it has also been found in the turkey and peacock.

Of domestic animals the sheep, ox, and pig are the principal intermediate hosts of the larval or bladder stage.

It has been proved, by feeding experiments conducted with all necessary precautions, that hydatid bladders or scolices from sheep and cattle when administered to dogs produce *Tænia echinococcus*—and *Tænia echinococcus* only—in the intestines of the latter. Similar results have followed the administration of hydatids or scolices obtained from man.

It has been also experimentally proved that proglottides or ova of *Tænia echinococcus* administered to some at least of the domestic animals give rise to bladder-worms.

The conditions favourable to the prevalence and spread of hydatid disease appear, therefore, to be the following:—

1. Many dogs infected with *Tænia echinococcus*, by which means the supply of ova is kept up.
2. Many animals, such as the domestic herbivora (and in Australia the kangaroo), capable of serving as the intermediate host of the bladder-worm.
3. Conditions favourable to the entrance of the tænian ova into the alimentary canal, either of man himself or of the ordinary intermediate hosts.
4. Facility of access of dogs to the carcases or hydatid containing organs of the intermediate hosts, such as the domestic herbivora, by which means the supply of *Tænia echinococcus* is kept up.

So far as they go, statistics show that these prescribed conditions are actually fulfilled in localities where hydatid disease is most prevalent. As will be seen later, Iceland and Australia stand out pre-eminently in this respect; especially certain parts of the latter.

An estimate of the number of dogs to the population in various localities gives for England one dog to fifty inhabitants; for France one to twenty-two; Belgium one to eighteen; Iceland one to eleven (13), a proportion for the latter country increased by Krabbe to one to three or five inhabitants. There is, of course, greater uncertainty as to the proportion of dogs affected by the tapeworm; but of 100 dogs examined by the latter observer in Iceland twenty-eight were found to contain them.

According to Davies Thomas, the relative numbers of the domestic herbivora in Europe as a whole were estimated in 1881 to be sixty-six sheep and thirty horned cattle for every 100 inhabitants; while the corresponding numbers for Iceland, as quoted by Krabbe, were 488 and 36 respectively: Dr. T. Hjaltalin estimated that evidence of hydatid infection was to be found in every fifth sheep.

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[1] Dr. Manson has pointed out that in India the jackal is in intimate relation with man, being a constant visitor in all towns and villages.

[2] A species of Arctocephalus that died in the Zoological Gardens, Adelaide.

In Australia, though an estimate might be made of the number of dogs registered in the settled districts under the various Dog Acts of the colonies, such a record would leave out the enormous number, both in settled and outlying districts, which does not come under this head. There is no doubt, however, that the proportion of dogs to population is very great, and possibly exceeds that of Iceland. If the dingo should prove to be a host of the tapeworm this proportion would be greatly increased.[1]

A more accurate estimate can be made of the number of sheep and cattle. The official returns of the various colonies show that in 1892 there were in Australia as a whole about 3000 sheep and 300 horned cattle for every 100 inhabitants. No data, however, exist for any precise statement of the proportion affected with the bladder-worm, but it is certainly large. Of 50 sheep examined, 22, or 44 per cent, were found infected in one or more organs.

We shall consider the conditions which favour the entrance of the tænian ova into man or the domestic herbivora, and conversely of the bladder-worms into dogs, as they exist in Australia, with which country we are most familiar.

The explored parts of the country are stocked more or less heavily with sheep and cattle; many districts are overrun by dogs, not only by the dingo, in which, as has been said, the existence of *Tænia echinococcus* has not been demonstrated, but by domestic dogs that have "gone wild," and by cross-breds resulting from the interbreeding of these. Large packs of such mongrels accompany every wandering band of aboriginals.[2]

The result is that an enormous destruction of stock takes place in spite of the costly, though too often spasmodic efforts in the direction of "vermin destruction"; it must be remembered also that the kangaroo is an intermediate host, but its numbers have largely diminished in recent years.

Moreover, in the vicinity of bush habitations the offal of the carcases used for food-supply is too often carelessly thrown aside, and affords frequent opportunities for the bladder-worms to reach the intestines of the dog; the abundant ova of the resulting tapeworm, deposited with the fæces on the ground or herbage, or reaching the water-supply, may in their turn find their way into the bodies of the intermediate host.

In the water-supply, in fact, we probably have the explanation of the chief source of infection of man himself. In many parts of Australia this consists largely either of permanent swamps (as in certain parts of Victoria and South Australia where hydatids are particularly common), or, more frequently, of water-holes, natural clay-pans or excavated reservoirs, all of which, after rain, receive the washings of the surface. Not only do the dogs have access to these surface collections, often obviously contaminated, but the water is drunk both by man and beast—by the former frequently and sometimes of necessity—with as little precaution to reduce the risks of infection as by the latter.

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[1] In South Australia alone 7481 dogs, mostly dingos but partly cross-breds, were destroyed in 1893 under the Vermin Acts. Of unregistered dogs at least 40 per cent were found affected with *Tænia echinococcus*.

[2] It is remarkable that apart from accidental death and tuberculosis, no aboriginal inmate of the Adelaide Hospital has died from any other cause than hydatids.

Again, the use of imperfectly cleansed raw vegetables, in places where these are liable to be contaminated by the excreta of dogs, must be considered as a potential or actual source of infection.

When one remembers the affectionate familiarities with which pet dogs are treated, and the habits of dogs among themselves, it is not possible to ignore these animals as a cause of direct infection. Dr. Thomas, our late colleague, relates a case in which it is highly probable that a very young child contracted hydatids in this way.

It may be well, perhaps, to state here that there is no evidence to support the commonly expressed belief that the contents of echinococcus cysts themselves, when they occur in animals used as food, may, if ingested, give rise to hydatids in man.

In Iceland, with which one of us is also familiar, though the physical conditions are widely different, yet there are the same necessary factors—many dogs, many herbivora, and contaminated pasturage or water; moreover there is in that island a closer bodily association between man and beast, and greater uncleanliness in person and in the use of food.

Geographical distribution. — Though hydatid disease occurs in many countries, the published statistics, so far as known to us, do not permit of very precise statements of its comparative frequency; this is perhaps more true of the old world than the new as represented by America and Australia, the great prevalence of the disease in the latter country having compelled attention to it.

Quite uninfluenced by climate in itself, the spread of the disease appears to depend entirely upon the degree to which the factors mentioned in the preceding section are present.

Dealing first with Iceland and Australia, the two chief homes of hydatid disease, the absence of comprehensive statistics invalidates all numerical statements; still, enough evidence is forthcoming to support the general tenor of the previous statement as to the remarkable prevalence of the disease.

Iceland.—Estimates of the total number of the population affected vary from $\frac{1}{16}$th to $\frac{1}{58}$th. If we suppose the former to be too high an estimate, the remarkable frequency of the disease is evident nevertheless. Thus Schleisner, who seems to have been the first to indicate the parasitic nature of a disease that had long been known in the country under such names as infarctus, hepatalgia, obstructio, or hypertrophia hepatis, found that about $\frac{1}{8}$th of the 2600 sick who appeared in the medical reports of the island, and $\frac{1}{6}$th of the 327 sick under his own immediate care, were affected with hydatid disease. On the other hand, Dr. Finsen, after nine years' experience, states that of 7539 cases 280, or nearly 1 in 27, suffered from hydatid disease. This latter figure accords sufficiently nearly with the estimate by Galliot, that the number of the population affected may be reckoned at about $\frac{1}{30}$th.

Australia.—Although Australasia as a whole enjoys an unenviable reputation for the prevalence of hydatids, this disease does not by any means occur with equal frequency in the several colonies, or even in all parts of the same colony. Whether reckoned on the basis of the ratio of the registered deaths from this cause to the total mortality, or on the proportion of the admissions of persons suffering from hydatids to the total number of patients received into the various hospitals, the disease is found to be most frequent in South Australia, somewhat less so in Victoria. New South Wales, Tasmania, Western Australia, New Zealand, and Queensland follow with a diminishing ratio in the order named. This statement is based on returns up to the end of 1894, covering over half a million of cases of admissions to various hospitals. The region of Australia, however, which yields the largest proportion of cases is that which comprises the south-eastern part of South Australia and the contiguous western district of Victoria—a well-stocked and comparatively cool region which includes much permanent surface water, often in the form of swamps. The returns, extending over many years, of the Mount Gambier Hospital, situated in one of the swampiest parts of the district, show one hydatid patient for every sixty-five admitted for all complaints; these figures are probably not exceeded in any other locality. It is remarkable, however, that no case of the multilocular form has been recorded in any of these colonies.

Great Britain.—Cobbold and others, who have endeavoured to ascertain the degree of prevalence of hydatid disease in the United Kingdom, have found a difficulty in basing any reliable estimate upon the defective data provided by the returns of the Registrar-General's department. (We should add that we are referring to a period prior to 1880.)

The circumstances under which we write have made it impossible for us to investigate the later years either of the Registrar-General's or of hospital statistics; thus this section of our article must be necessarily incomplete. Nevertheless the following statements may be taken for what they are worth:—

Thomas quotes figures, derived from the Registrar-General's statistics for the decennial period ending 1880, which show one death from hydatids to 11,876 deaths from all causes. As the result of a special inquiry addressed by the same writer to various British hospitals (replies having been received only from the London Hospital and one other), it was found that in the former institution, during a period of five years, twenty-four cases of hydatid disease were treated out of a total of 13,297 *medical* in-patients—a proportion of 1 to 554; while from the published reports of three Metropolitan hospitals—St. Thomas's, St. Bartholomew's, and St. George's—he derived, from the aggregate of figures, a corresponding ratio of 1 to 1124, the proportion varying considerably in the several hospitals.

Dr. Murchison reports that among 2100 necropsies at the Middlesex Hospital between 1853 and 1863 hydatids were found in thirteen instances only; that is, one in 161 cases. He further states, as the result of investigations at the Royal Infirmaries of Edinburgh and Glasgow, that hydatids are much rarer in Scotland than in England.

The limited area to which these various figures apply, and the wide discrepancies in them, render them of little value. Still here and there a useful comparison may be made with other statistics.

In *Germany*, and, according to Leuckart, in the central and northern parts especially, the disease is not infrequent. So also it occurs, but with probably less frequency, in *France*, *Austria*, *Russia*, *Italy*, and other European countries. It is remarkable that a very large proportion of the recorded cases of *Echinococcus multilocularis* are from *Switzerland*. Hydatid disease occurs also in *Egypt* and *Algeria*.

British India.—From the infrequent reference to hydatid disease by Indian medical writers, it would appear not to be of common occurrence in this country—an opinion supported by the result of some inquiries made by the late Dr. Thomas. On the other hand, Hirsch states that the parasite is of somewhat frequent occurrence in India, a certain proportion of the endemic hepatic abscesses of that country being stated by Cleghorn to be referable to it.

In *China* hydatids must be extremely rare, for we have it on the authority of Dr. James Cantlie of Hong-Kong that, out of upwards of 40,000 cases seen by him in that country, one only was of this nature; it occurred in a European, and apparently was not of endemic origin.

In *North America* the disease is decidedly uncommon; Osler in 1882 was only able to record sixty-one cases for the whole of the United States and Canada.

Age markedly affects the incidence; for, though the disease has been met with in a child two years and one month old, and in a man of eighty-one, the mortality from hydatids in the Australian colonies, compared with that from all diseases, rises continually through each decade of life till fifty years of age, and then gradually falls again.

Sex.—Out of returns covering 2307 cases of hydatid disease occurring in Australia in which the sex was clearly indicated, 1300 were males and 1007 females—a ratio of 100 to 77 (returns to 1894 inclusive). This increased liability of males is probably the rule; and is, no doubt, due to the occupations of men, and their predominance in numbers over the opposite sex in regions where the conditions are most favourable to the existence of the disease. Still, an exception appears to exist in the case of Iceland, where it has been stated that more than twice as many women as men have the disease. In Iceland the habits of life of the people are such as to expose women more to infection.

Pathological anatomy.—The general features and varieties of hydatid cysts have been briefly indicated in the relation of the life-history and development of the parasite. In this section (in which we have been much aided by our colleague, Professor Watson, pathologist to the Adelaide Hospital) it is proposed to add a few details.

It is admitted that there is only one true larval species of echinococcus, and that the special characters of the surrounding tissues, in which the hexacanth embryo has come to rest, exert a determining influence on its further development in respect of its size, shape, and mode of reproduction; or, in other words, on the special characters which it assumes.

In man the most usual form is that of a mono-cyst developed from a single embryo; a plurality of such cysts often coexists in the same individual, or even in the same viscus (multiple hydatids); and is referable to separate and not necessarily simultaneous parasitic invasions. In man such cysts often attain an enormous size, and, as we have shown, may give rise to a numerous progeny of daughter or even granddaughter bladders situated internally.

The less common form is that in which the original cyst, resulting from a single embryo, by repeated external proliferation produces a more or less compact cluster of vesicles, which are always comparatively small, and often very minute; in the multitude of these the identity of the parent cyst may be lost.

This type includes Virchow's multilocular or alveolar form, which, by the feeding experiments of V. Klemm, has been identified as the product of the same larval species as other echinococcus cysts (14). It is possible that those rare cases where, a mother cyst being absent, a plurality of vesicles occupies a common cavity, and may be adherent to its walls, belong also to the exogenous type.

The adventitious capsule.—An aseptic foreign body embedded in an organ excites by its presence a cell proliferation in the surrounding connective tissue; the presence of a similarly situated parasitic cyst evokes a like response. The pressure induced by its continuous expansion, however, calls into existence an opposing factor which antagonises the tendency to cell proliferation; and, by a maintenance of equilibrium between irritative hyperplasia and pressure atrophy, the capacity of the capsule increases step by step with that of the essential cyst. Nevertheless it must be admitted that in certain cases all signs of irritative hyperplasia are absent; and that as an aseptically detached appendix epiploicæ excites no reaction in the peritoneal cavity into which it falls, so an echinococcus vesicle may remain naked and free.

Again, around hydatid cysts situated in well-protected parts, such as the brain, lungs, or bone, the capsule, if not entirely wanting, is represented by a condensation and survival of but a small portion of the pre-existing connective tissue. On the other hand, in more exposed situations it may attain a considerable thickness.

In structure the adventitious sac is, in juvenile cysts, both cellular and vascular. In older living cysts it is formed of fibres and flattened cells arranged in concentric laminæ, which, as the inner surface is approached, become fused, condensed, and more or less destitute of cellular elements. The inner face of a healthy sac is smooth and of a faint pink colour, but we have not been able to satisfy ourselves of the existence of the alleged internal cellular layer. So also, though in young cysts a certain amount of vascularity may be noticed, we have not, in a large series of cases, observed the varicose condition of the capsular vessels which has been said to give rise to dangerous bleeding after removal of the essential cyst. Indeed this event, beyond a slight hæmorrhagic leakage, has been absent from our experience.

The shape of the sac, to which that of the enclosed parasite corresponds in virtue of the internal pressure to which it is subject, tends to assume a spheroidal form; when, however, its uniform expansion is interfered with by inequalities in the density of the surrounding tissues, it acquires a more or less irregularly sacculated shape. If the mutual pressure of adjacent parasites upset the equilibrium between hyperplasia and atrophy in the intervening partitions, the sacs coalesce into a compound sacculated capsule in which a separate parasite occupies each pouch. When the unequal resistance of surrounding parts is supplemented by a special inherent tendency of the parasite to grow in certain directions, a compound sacculation, extending even to separation, ensues, such as is seen in the multilocular form.

Extra capsular effects of the growth of the parasite.—The connective tissue of the affected viscus survives the more highly organised parenchymatous elements, such as the liver-cells, etc.; but in the uninvaded parts the latter undergo a compensatory hypertrophy. When the growing parasite comes to abut on the serous capsule of the viscus a fusion of its own adventitia with the latter takes place, and the combined structure may become further adherent to other neighbouring serous surfaces.

Degenerative changes in the capsule.—With increasing age the adventitious sac is apt to undergo degenerative changes; these may be of an aseptic character, such as sclerosis or even calcification, due to the deposition of lime salts—phosphate and carbonate; or the latter condition may lead to the formation of foci of a degraded kind of bone. Usually these changes do not affect the capsule uniformly, but occur in patches of varying size, and may lead to enormous thickening. In a recent case of splenic hydatid at the Adelaide Hospital this calcareous and, to some extent, osseous transformation had proceeded to such a degree that the use of a small saw was necessary to effect an opening.

Again, changes of a septic character may take place, either spontaneously from unexplained causes, or as the result of surgical interference. Thus we may have suppuration, ulceration, putrefaction with evolution of gas, and even gangrene.

Being a product of the connective tissue of the host the capsule may be invaded by pathological changes affecting the viscus in which the parasite is embedded; in this way it has been affected by carcinomatous and lardaceous disease.

The Echinococcus bladder.—The structure of this organism has already been described. The lamination of the elastic cuticle, or ectocyst, a characteristic feature of the bladder-worm even at a very early stage, becomes with increased age still more conspicuous by the formation of fresh layers; till, in the mother cyst, it may reach a considerable though not necessarily a uniform thickness. So characteristic, indeed, of hydatid cysts is this structure that the discovery of a minute fragment, which, in the absence of all other definite products, may be obtained by the hypodermic needle, renders the diagnosis absolutely certain. In chemical composition it belongs to the class of substances known as chitinous.

The fluid which occupies the interior of both mother and daughter bladders, and keeps their elastic walls at a considerable degree of tension, is a limpid, colourless, transparent, neutral and feebly opalescent liquid having a specific gravity of 1006 to 1015, and containing from 1 to 2 per cent of solids, amongst which albumins are either wholly or almost wholly absent. Minimal quantities of sugar, inosit, kreatin and urea may exist with some inorganic salts, of which chloride of sodium is the most conspicuous. A poisonous ptomaine has been detected by Mourson and Schlagdenhauffen (11). In the contents of dead or dying cysts there may be serum, bile or blood. The withdrawal of a transparent fluid, therefore, which yields to the ordinary tests no albumin, or but a trace, and gives a copious precipitate with argentic nitrate, affords strong evidence of its derivation from a hydatid cyst; but, as elsewhere stated, on account of the identical appearance and reactions of some other normal or pathological fluids of the body, absolute reliance cannot, in certain cases, be placed upon these tests alone; and the detection of one or other of the biological products then becomes the only certain means of determining the parasitic nature of the tumour. Sometimes these are not forthcoming,

Causes of spontaneous death.—Dead hydatids are found more frequently in the liver than in other parts, both because the liver is the most frequently affected viscus, and because spontaneous evacuation *per vias naturales* is less easily effected than in viscera such as the lung and kidney.[1] Echinococcus cysts may die at any stage of their existence; and it is possible that, like other living things, they die on attaining a certain age. As a rule, however, disturbances of the obscure relations existing between the parasite and the tissues of their host anticipate the natural term of their life.

Several theories of the possible causes of natural death, all more or less unsatisfactory, have been suggested. It is said, for instance, that malnutrition, induced by diminished blood-supply, entails an aseptic death of the parasite; more especially when the latter has taken up its abode in the peripheral portions of an organ where the blood-supply is necessarily poorest.

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[1] Out of thirty-six cases which, on autopsy at the Adelaide Hospital, were found affected with hydatid disease of the liver, ten were the subject of retrogressing cysts that had been unsuspected during life.

Irruptions and transudations of the normal fluids of the body, such as blood, serum, bile or urine, are adduced as mechanical and toxic causes of death.

Static shrinkage of the capsule, inordinate growth of an internal brood, are said to lead to a disproportion between the carrying capacity of the capsule and the contained parasite, which is inimical to its further development.

Whatever the causes of death, however, it is possible that they may be local rather than general, as the same individual may be the subject of both dead and living hydatids; even in the same viscus there may be cysts in widely different stages of degeneration, indicating death at different periods. Due weight must also be assigned to the suggestion that oft-repeated or long-applied traumatism, such as the continuous riding on horseback of bushmen, or perhaps, again, the toxic effects of the continuous use of noxious fluids as beverages, may eventually prove fatal to the life of the parasite.

The effects of *rupture of hydatid cysts* into various cavities and passages of the body, or even externally, will be described in the clinical section. They lead sometimes to spontaneous elimination of the parasite and a consequent relief of the host; but more often to urgent symptoms which require prompt surgical interference. Rupture of a healthy bladder may result from undue compression or other violence; or from pressure atrophy, due to expansion of the cyst, the thinned intervening tissues giving way at the weakest spot; but most frequently it is the consequence of localised ulcerative changes in suppurating cysts.

Hydatid cysts that die and undergo spontaneous retrogression become the subjects of a very constant series of degenerative changes, which may be described in the following stages:—

1. *Stage of turbidity.*—The fluid of the mother cyst becomes turbid from the precipitation of the albumins of the nutritive pabulum, which, being no longer absorbed and metabolised by the dying or dead parasite, are suspended in the fluid, causing it to become albuminous. A similar transudation of serous fluid and refilling of the sac, or possibly of the cyst itself, may take place after tapping. Thus far there are no changes in the adventitious sac, and the contents of the daughter cysts are still clear.

2. *Fatty stage.*—These precipitated proteids are converted into fatty substances resulting in still greater turbidity of the fluid; at a later period the liquid contents may assume the consistency of a butter-like smegma. The mother cyst acquires a gelatinous or gummy aspect; the daughter cysts shrink, and their contents in turn become turbid. Though

the daughter cysts undergo precisely the same series of changes as their parent, the former are, generally speaking, a stage behind the latter in their transformations.

3. *Stage of desiccation.*—There is complete opacity and marked desiccation of the contents, which are represented by a putty-like mass. Degeneration has proceeded in the mother cyst, which has now become a mass of gelatiniform shreds not yet completely opaque. The fatty transformation has extended to the production of crystals such as of stearin and cholesterin, and less frequently of other crystalline forms of obscure nature and uncertain composition; among these Charcot's crystals may be mentioned.

4. *Stage of calcareous infiltration.*—Infiltration of lime salts—carbonate and phosphate—which has previously begun in the adventitious capsule, becomes general in the whole mass. The putty-like substance slowly disappears with a corresponding shrinkage, and the parasite is now represented by a semi-calcareous mass in which are embedded the shrivelled and opaque remains of the mother and brood.

In a further stage, seldom reached, even these membranous débris may lose their identity, the hooklets only remaining to indicate the true nature of the now wholly calcareous mass.

Presence of bilirubin.—In a certain number of cases of liver hydatids the mother cyst, its liquid contents, and—at a later stage—the daughter cysts also, may become stained a green or orange colour from irruption or transudation of bile, which most frequently takes place between the adventitia and the mother cyst, though it may involve the latter. When this is in excess it may give rise to the presence of amorphous masses of biliary matter or of bilirubin crystals. In one case—an enormous cyst of the liver which had begun to suppurate—we found a mass of crystalline bilirubin, with traces of biliverdin, weighing 1·13 gramme; many of the daughter cysts were stained with a similar material. So far as we are aware, this substance has not been found in cysts other than those of the liver, a fact which indicates its biliary origin; further, in our experience, it occurs only in those cases where the parasite is dead. In hydatids of the kidney crystalline products referable to the urinary secretion have been found.

Papillomatous growths in hydatid bladders.—Besides the above series of changes, which constitute what may be called the usual pathological sequences of spontaneous death, various observers have noticed, projecting from the inner wall of cysts otherwise apparently normal and containing large broods, peculiar raised papilloma-like excrescences, which occur in scattered patches of over an inch in diameter and of 2 mm. or more in height. Microscopically they consist of hypertrophic ingrowths, rather than infoldings, of the cuticle; and in one case they contained small daughter cysts with relatively thick walls. We have observed these papilloma-like growths in cysts which were diagnosed as belonging to the lung, liver, spleen, and brain. Probably they represent abortive efforts at endogenous proliferation. In some of these cases patches of the mother cyst were gelatiniform and of a transparent amber colour, as if vitality were lost and degeneration about to become general.

Absence of mother cyst.—Hydatids occasionally occur, in which, with every appearance of endogenous development, no trace whatever can be found of a mother cyst. It is difficult to understand by what processes so substantial a membrane can be completely absorbed, macerated or dissolved; yet this seems the only kind of explanation that can be offered. Such an example was an enormous hydatid in the liver of a male subject, the contents of which measured 20 pints. On a calculation, based on an enumeration of the daughter cysts in a measured quantity, the total number of these exceeded 28,000; and this figure did not include thousands that were too small to be counted with the naked eye. Suppuration had not long commenced, but not a shred of mother cyst could be detected. It was in this case that the aforesaid crystalline mass of bilirubin was found. The man recovered after incision and evacuation, and about three years afterwards was again successfully operated on, in a similar manner, for another large hepatic suppurating cyst, containing five pints, which presented no unusual features.

The unequal distribution of hydatids in the various viscera requires a short discussion of the circumstances which determine the ultimate destination of the wandering embryos. The conspicuous preponderance of liver cysts is attributed to a passive transportation of these embryos by the blood of the portal vein. The still large, but lesser, relative frequency of pulmonary hydatids is, on the same vascular transportation theory, generally explained by the fact that the travelling embryos can only reach the lungs after traversing the portal capillaries; and the still less frequent presence of the parasite in other organs finds a similar explanation in the fact that the embryos on their way must traverse both the portal and pulmonary circulations.

It is difficult, however, on this theory to account for the comparative frequency with which multiple peritoneal and omental cysts are found; for we must then believe that these cases owe their origin to an arterial embolic shower of embryos which have successfully traversed the two capillary obstructions of the liver and lungs—unless we may suppose that they either work their way into the omental arterioles or enter the radicles of the omental veins, in which latter case they would have to reach their destination against the venous blood current. Now it often happens that the lungs have entirely escaped invasion, while a multitudinous cystic development is in progress in the peritoneum and omentum, an event which would not be probable if the embryonic swarm had passed through the lungs; we can only suppose that it is possible for embryos, after having traversed the stomach, to reach the peritoneal cavity by gravitation or otherwise, there to develop into cysts which acquire their capsules by exudation from this membrane, and doubtless multiply by exogenous proliferation. It is noteworthy, however, that the peritoneum does not always respond to the presence of the parasite in the same active manner, for the bladders may fail to acquire any adventitia, and thus remain entirely nude and free in the peritoneal cavity. Indeed, when we review the facts of distribution of this and allied parasites, as well as the failure to account for them satisfactorily by vascular transportation or other passive migration, we are disposed to lay the greater stress on a selective affinity, which seems to lead the parasite to certain situations. A like phenomenon is a special disposition, possessed by certain nude hydatids, to enlarge independently of the plane of least resistance, or even in direct opposition to it. In this way cerebral hydatids may perforate the bony cranial vault—an event which has its parallel in the behaviour of the cœnurus, which in a similar way perforates the skull of sheep, and so offers facilities for cure by puncture.

It is necessary, however, to bear in mind that the external appearances of a cerebral hydatid may be exactly simulated by a parasite of the cranial bones, which has caused absorption and thinning of their substance.

Even in the case of the liver another view than that of passive transference is possible, for it is possible that the embryos may bore their way directly from the one organ to the other.

Although there is, we believe, no direct experimental evidence in favour of the view that scolices, brood capsules, or even daughter bladders may, when they escape from a parent cyst into a serous cavity, give rise to a crop of multiple hydatids,[1] yet, when we remember the difficulties of other theories of transit, this supposition seems reasonable in the light of certain cases in which the peritoneum and peritoneal surfaces of the abdominal organs, often in the most dependent positions, have been found studded with innumerable small cysts of such uniform size as to suggest a sudden and simultaneous invasion in this manner. In support of such a view, it has been pointed out by Graham that in some of these cases there had been an antecedent tapping of the cyst, a warning of great importance to the surgeon.

General Clinical Aspects of Hydatid Disease

Before proceeding to describe the symptoms, physical signs, diagnosis, and treatment of hydatids in the different organs of the body, there are certain general considerations, applying to hydatids wherever situated, which may be advantageously discussed.

Symptoms.—In conformity with the comparatively slow growth of the parasite the surrounding parts usually so accommodate themselves to its presence that, even when of great size, it may occasion surprisingly little inconvenience. There may be a sense of fulness and weight, and an interference with certain movements of the body. Severe pain is accidental, and due generally to irritation of a nerve-twig by the enlarging capsule. Sometimes the pain is inflammatory in character, as when a pulmonary hydatid approaches the pleura and excites a localised pleuritis, or a hepatic hydatid a similar peritonitis. At times a living hydatid is found in the substance of a lung, the seat of lobar pneumonia; in this case the same pain and other symptoms arise as when the pneumonia is primary, and it is impossible to say whether it be due to the presence of the parasite or is an accidental complication.

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[1] Naunyn and Rasmussen have asserted that scolices and brood capsules do sometimes change into hydatids, (10) p. 634.

Symptoms due to interference with the function of an organ in which a hydatid is situated vary inversely as the ability of the organ to expand. If the organ can increase in size step by step with the growth of the parasite, as in the liver or spleen, there is very little destruction of tissue in its neighbourhood; and this may be balanced by hypertrophy elsewhere: the parenchyma is pushed aside, and so slowly as to permit of adaptation to its new conditions, with little or no diminution of its function. In the lung, which is confined within moderately resisting chest walls, as the parasite enlarges the breathing space diminishes; for the lung retracts as the growth relaxes the elastic pulmonary tissue. When, however, the retraction is complete, and the growth begins to exert a distinct pressure on the chest wall, this will yield before its advance, and bulge so considerably that the diminution of lung space will be less than the increase in the size of the tumour. Where, as in the brain, no expansion of the viscus is possible, pressure symptoms soon arise, though even here marked adaptation may take place; thus, in children, brain hydatids acquire a much greater volume without issuing fatally than in adults. When operated on they have been found to hold more than a pint of fluid, the bones of the skull having become so widely separated at their sutures as to allow the head to become very voluminous; or the bones may have yielded and enlarged, so as to produce a very noticeable prominence over a large area.

After a hydatid cyst has been punctured for purposes of diagnosis or treatment, an urticarial rash often follows within a short time. This is usually general, and lasts for a few hours or one or two days. It has also been noticed after the rupture of a hydatid cyst into one of the large serous cavities. It is probably occasioned by absorption into the blood of a poisonous ptomaine present in normal hydatid fluid. So also a form of localised urticaria, or even a mild cellulitis lasting for one or two days, may arise from escape of fluid into subcutaneous tissue after puncture of a superficial cyst. On suppuration of the adventitious capsule the symptoms are those of a large abscess of the organ infested by the parasite; namely, pyrexia, varying in its intensity in different patients though generally of a remittent type, with its several concomitants, headache, general pains, anorexia, furred tongue, and so on; sometimes there are repeated rigors, local pain and tenderness, and a continuous increase in the size of the tumour or organ detectable by careful examination. Suppurating hydatids have a marked tendency to rupture, or rather to open into neighbouring cavities; the symptoms, under these circumstances, vary with the direction of the rupture, whether into a bronchus, the bowel, the peritoneum, the pericardium, the urinary passages, or elsewhere.

Physical signs.—On inspection there may be a slight but general bulging of the part, a markedly smooth and round local prominence; or, if the parasite be multiple, a number of bosses may exist. On palpation the tumour is found to be smooth and firm, sometimes elastic; in other cases it is quite hard, as though solid. Fluctuation can seldom be detected in hydatid tumours owing to their high tension. On percussion they are absolutely dull, and in a certain proportion of cases yield a hydatid thrill. This is a peculiar vibratory sensation perceived by the finger percussed, which when the cyst is large may be elicited over a considerable area. It is not, however, always detectable—in fact, the proportion of hydatids in which it is present is comparatively small. Moreover, the same sign may be recognised in other cysts not hydatids, such as hydronephroses. Probably, for its production, the cyst must be of a certain magnitude, its contents of a certain density, its wall of a certain thickness and tension, and its attachments to surrounding structures definite. These associated factors are more frequently found in hydatid cysts than in any others, hence the sign is most common in them; but even in them they are generally absent, and the sign is therefore unusual. While, therefore, thrill is highly suggestive of hydatid, it is not pathognomonic; nor by its absence is the hydatid nature of a cyst disproved.

Diagnosis is often easy; at times it is difficult, or even impossible. A rounded, firm, smooth, elastic tumour in an organ or part, without antecedent or present symptoms other than those due to its size, and yielding a thrill on percussion, is most probably a hydatid. The probability is increased in countries, such as Iceland and Australia, where the disease is very prevalent. This element of geographical distribution cannot be ignored. In Australia, for instance, the disease, under the most unexpected conditions and from the most unlikely quarters, is continually springing surprises upon the physician; so that hydatid has constantly to be borne in mind. If the parasite be in the centre of an organ, this may be uniformly enlarged without a trace of local bulging; but examination of its contents may at once settle the question of diagnosis. A hypodermic syringe, with a needle from two to three inches long, or a fine aspirator needle, should be employed, and only a small quantity of fluid withdrawn. In a tumour even of considerable magnitude, when the mother cyst is closely packed with very small daughter cysts, the needle may draw off the contents of only one of these, a quantity so small as to be overlooked, especially if a large aspirator vessel be used; the growth may thus be mistaken for a solid tumour. If scolices, or hooklets, or a piece of membrane be visible under the microscope the diagnosis is final. Sometimes a fragment of cyst, quite large enough to determine the existence of the parasite by its characteristic lamination, may be blown out of the needle upon a slide.

Frequently none of these products are obtained, and we have then to depend on the character of the fluid. Unfortunately, as we have said, there are two liquids with which hydatid fluid is identical in appearance, and nearly so on chemical analysis — the cerebro-spinal, and that of some hydronephroses. When, on cerebral symptoms pointing somewhat indefinitely to an intracranial hydatid, the skull has been trephined and fluid withdrawn by a long hypodermic needle, it is a matter of serious moment, in regard both to treatment and diagnosis, to determine whether this has come from a dilated ventricle or from a hydatid. In the latter case an opening should be made in the brain substance for the removal of the parasite; in the former such a proceeding would most likely prove fatal. We have no test at present to decide the question; both fluids are clear and watery, both contain salt and a trace of sugar. The same difficulty arises in respect of a renal cyst. Though many hydronephroses contain fluid evidently urinous, some yield a liquid exactly like hydatid fluid. If we are sure that the cyst lies in the substance of the liver or spleen the exhaustion of fluid of a clear watery character decides the diagnosis; but we cannot always be sure of the situation of the cyst, for a right hydronephrosis is sometimes adherent to the under surface and margin of the liver, and at times the physical signs leave us in doubt whether a tumour in the left hypochondrium and anterior lumbar region be in the left lobe of the liver, in the spleen, or in the kidney. When the lung is in question it might be thought impossible to err. But here we are again confronted by a special difficulty. Numerous instances testify to the possible danger of the withdrawal even of a small quantity of fluid from a pulmonary hydatid. In consequence of this trifling operation the cyst may burst, and the contents, rushing up the bronchial tubes, may flood both lungs and drown the patient. Even if this fatal catastrophe should not occur, a most violent suffocative cough may be excited, followed by expectoration of blood and such quantities of hydatid fluid as utterly to prostrate the patient, even within a few minutes. On this account we lay down the rule, that no medical man should ever use a needle in his consulting-room to make a diagnosis in a possible pulmonary hydatid; nor should he attempt elsewhere to draw off the fluid without having all preparations complete for immediate incision and drainage if its hydatid nature be established. It is, however, quite justifiable and harmless, prior to incision, to insert a fine hypodermic needle, and draw off half a drachm or so of fluid, which will be enough to supply evidences enabling us to distinguish between a pleural effusion and a parasite.

Prophylaxis.—The general nature of the measures calculated to prevent or at least to limit the spread of hydatid disease becomes evident from what has been said concerning the conditions which give rise to it. As the prevalence of the parasite in man depends primarily upon the number of dogs affected with *Tænia echinococcus*, and the facilities afforded for the entrance of the ova into the human body, it follows that laws which require registration of dogs, and the destruction of those which are not registered, are of the greatest service if vigorously enforced. These laws not only usefully restrict the number of all dogs, but also serve especially to limit the class of vagrant or ownerless dogs which, in the absence of regular feeding with wholesome household scraps, are liable to be infected by the offal of butchers' shops or abattoirs. The offal of such establishments should, in fact, be so disposed of that dogs cannot possibly obtain it. A further safeguard would be to abstain from feeding dogs with raw meat of any description; for the usual culinary methods of preparation are destructive to the life of the bladder-worms should they exist. Judicious cathartic and anthelmintic medication of dogs might also be of service, but it must be remembered that any such treatment must be accompanied by such a disposal of the excreta as will prevent further infection. Indeed, similar sanitary precautions should invariably be taken to render innocuous, by boiling water or other means, the excretions which accumulate about kennels or other places where dogs congregate.

The water-supply being, as we have said, the principal source of the disease in man, all those measures are efficient prophylactics which protect it from contamination with the tapeworm ova, which are liable to be blown into it by the wind, or carried thither by the washings of the surface. Boiling or effective filtration of the water may be regarded as absolute safeguards, and too great care cannot be taken in the cleansing of those ground vegetables which are eaten raw. It has been suggested that the ova may gain entrance into the lungs with the inspired air. In Australia, at least, where the facilities for infection exist to so great a degree, and where dust-storms are frequent, it is possible that such minute bodies as the ova might in this way gain entrance to the body; it is even conceivable that the secretions of the air-passages might possess a sufficiently corrosive or solvent action to liberate the contained embryo; but direct proof is yet wanting, and we may probably with safety regard the alimentary canal as the only channel of entrance to the body. We repeat that the bad habit of kissing pet dogs is dangerous in respect of the possibility of direct transfer of hydatid from beast to man, disgusting in respect of some of the habits of the tribe.

It cannot be too emphatically stated that, for all practical purposes, the whole question of prophylaxis may be comprised in the statements, that if there were no dogs containing *Tænia echinococcus* there would be no hydatid disease; or that, if the source of supply of bladder-worms were entirely cut off, dogs would no longer be infested with *Tænia echinococcus.*

Treatment. — A great variety of remedial measures have been applied to hydatid disease, and these may be classified in two groups —those, namely, which aim at the destruction of the life of the parasite *in situ*, and those which aim at its removal.

1. Measures which aim at the destruction of the life of the parasite.

(*a*) *Internal administration of drugs.*—Of the various medicaments which have been used with this object it may be confidently asserted that they are absolutely useless.

(*b*) *Acupuncture.*—Long thin needles are inserted into the cyst, left there for ten or fifteen minutes, and then removed. This probably cures (when it does cure) by allowing the contents of the bladder to escape into adjacent cavities, such as that of the peritoneum in the case of the liver. Apart from the great uncertainty of the method, it is reprehensible on account of the possibility of a general parasitic invasion of the peritoneum by escaped scolices, a subject we have already discussed.

(*c*) *Electrolysis* probably acts not by virtue of the electric current, but of the acupuncture; and the practice is to be condemned accordingly.

(*d*) *Injection of fluids into the cyst after removal of some of its contents.*—The following have been employed:—Extract of male fern, carbolic acid, alcohol, solution of pepsin, potassic permanganate, tincture of iodine, mercuric chloride. None have proved efficacious.

(*e*) *Aspiratory puncture and withdrawal of fluid.*

2. Measures having the object of complete removal of the parasite.

(*a*) By means of an opening made with *caustics* (Récamier's method).

(*b*) Long-continued *drainage* and evacuation through a canula inserted into the cyst and retained for a long period (*canule à demeure*).

(*c*) *Double puncture with small trochars, followed by incision* (Simon's method).

(*d*) Various forms of *direct incision* with immediate or delayed removal of the parasite.

Of the several methods which have been enumerated two only require further consideration; the others are either inefficient, or open to other objections so serious as to have led to their abandonment. The two methods are aspiratory puncture and removal by direct incision. These we shall discuss a little more in detail.

Aspiratory puncture.—Under antiseptic precautions, and by means of an aspirator needle, which should not exceed one-sixteenth of an inch in diameter (results having shown conclusively the superior safety of a small needle as compared with larger sizes), as much fluid is drawn off as will flow. This simple and, as its advocates urge, safe procedure does undoubtedly cause the death of the parasite in a certain proportion of cases, and the consequent cure of the patient; indeed, this event may happen after withdrawal of a very small quantity of fluid, the dead organism then passing through the same kind of harmless retrogressive changes as it does when undergoing spontaneous cure. It must be remembered, however, that, although the aspiratory puncture may have caused the death of the parasite, the tumour may quickly regain its former size. If now a portion of the fluid should be again withdrawn it will be found albuminous, the sac (or cyst) having become filled with serum. Under such circumstances attempts to remove the fluid are very likely to induce suppuration, and it is advisable, therefore, that no further aspiratory puncture should be performed until after the expiration of twelve months. If, after the lapse of that time, serous fluid be still forthcoming it will be wise to leave the tumour alone; in all probability it will ultimately subside.

Notwithstanding the favourable results which have undoubtedly attended this method of treatment in many cases, some very serious objections are urged against it. In spite of its simplicity the operation is by no means devoid of danger; death has occurred from shock in a considerable number of instances, and extreme collapse, from which, however, the patient may gradually recover, is not infrequent. The operation is only likely to be successful in simple living cysts, or in those at any rate in which there are few daughter cysts—conditions which are quite undeterminable beforehand. In any case no assurance can be given that the operation will be successful, for the puncture frequently fails to kill the parasite or, still worse, leads to inflammatory or suppurative changes. Even if its life be destroyed it remains in the viscus a bulky, dead organism, prone to decomposition with all its mischievous complications. This method is quite inadmissible in suppurating or ruptured cysts, and is inadvisable, as we shall point out more fully, in all pulmonary hydatids.

The range of its application thus becomes very narrow; indeed, in Australian practice, based upon a large experience, there is a marked tendency not only to abandon aspiration altogether as a curative measure, but also as far as possible to limit its application even as a means of diagnosis.

Removal by incision.—The operations included under this head aim at removal of the parasite, either at once or after some little delay. The particular method known as Lindemann's operation has been successfully adopted by Australian surgeons for some years. In this procedure the bladder and its contents are removed at the time of operation by an incision made through the most prominent part of the tumour, or, it may be, at some other spot from which the parasite is more conveniently accessible. The edges of the visceral wound, if not already adherent, as is frequently the case, are attached by stitches to those of the parietes of the body, so that the cavity formerly occupied by the parasite drains externally. Rarely is any difficulty experienced in the dislodgment of the mother bladder, which readily presents itself in the wound, and, so to speak, invites removal; moreover, it is remarkable how soon enormous cavities close up by adherence of the collapsed walls or by granulation. More recently a plan, proposed by Mr. Bond of Leicester for abdominal hydatids, has been put in practice both by himself and other surgeons. In this, after the removal of the essential cyst, its cavity is carefully emptied, cleansed, closed by sutures, or even left unclosed; and the wound in the abdomen is closed over it as in an ovariotomy. Even suppurating cysts have been treated successfully in this way. Discussion of the various surgical procedures and details are, however, foreign to the scope of the present article, nor do its limits permit us to enter more than briefly upon the discussions of the relative advantages of aspiration and incision, which are practically the only procedures in use in the Australian colonies of late years.

By an appeal to statistics it is possible to contrast the actual death-rate of these two methods with some degree of accuracy; but such figures, though not unfavourable to the more radical operation, are by themselves very inconclusive. Aspiration is limited, even by its strongest advocates, to a restricted class of cases which, to say the least of it, does not comprise the severer forms; while incision, applicable to all kinds, is the only justifiable procedure in a large class of the severer cases of suppurating or ruptured hydatids to which, indeed, aspiration would be wholly inappropriate. Thus, any comparison based only on the death-rate of the two operations must take account of the difference of severity of the two classes of cases. Moreover, no estimate can be made of the undoubtedly large number of cases in which aspiration has failed in its object, or has itself been the cause of those inflammatory or suppurative sequels which increase the danger. So also from a pathological standpoint it is incontestable that the procedure which aims at the complete removal of a foreign organism is more sound in principle than one which at best leaves in place a dead organic mass with its potentialities for future mischief.

The following figures, derived from the records of the Adelaide Hospital (South Australia), where for some years Lindemann's operation has been almost exclusively performed, give numerical expression to the results that have been obtained.

During the seven years ending 31st December 1894, 121 incision operations have been performed on hydatids within the great cavities of the body, the aggregate result showing a total mortality of 16·5 per cent, as follows:—

[TABLE

TABLE.—Summary of Operations for Hydatids at the Adelaide Hospital from 1st January 1888 to 31st December 1894.

Position of Parasite.	Operation.	Results.		Total.	Percentage of Deaths.
		Cures.	Deaths.		
Hydatids of Pleura[1] . .	Thoracic Section	9	...	9	4·5
,, Lung . .	,, ,,	12	1	13	
,, Liver . .	Thoracico-abdominal Sections[2]	17	8	25	32·
,, Liver . .	Abdominal Section	51	7	58	13·8
,, Spleen . .	,, ,,	...	2	2	
,, Kidney . .	,, ,,	1	...	1	
,, Omentum .	,, ,,	6	1	7	
,, Broad Ligament	,, ,,	1	...	1	
,, Pelvis . .	,, ,,	3	...	3	
,, Kidney . .	Lumbar Section	..	1	1	
,, Peri-renal Tissue	,, ,,	1	...	1	
	Totals .	101	20	121	

Thirteen of the deaths, however, were in no way attributable to the operation,[3] and if it were permissible to deduct these the results would yield the much more favourable return of 5·8 per cent of deaths, a result which is decidedly encouraging for so severe a procedure.

The preceding table comprises only those operations which have been performed at the Adelaide Hospital, a homogeneous group which have been treated in a similar manner, and have come under our own immediate observation; but by the inclusion of other cases, of which we have particulars, the number operated on by this method might be raised to 285 with a death-rate of 16·4 per cent, without any deductions; or almost exactly the same as that of the smaller table.

Analysis of the whole series would show further that nearly all the fatal results occurred in those cases where suppuration had commenced. It cannot therefore be too forcibly pointed out that, as this event constitutes the most serious ordinary danger, prompt action is necessary, as well as the avoidance of any of those measures which may lead to this untoward result.

The following propositions indicate the principles of the treatment of hydatid disease that are generally accepted in Australia.

1. The objections to aspiratory puncture are that it is only applicable to a small class of cases; that even in these it frequently fails in its object; that it is in itself a possible source of danger, by inducing suppurative changes, or by permitting leakage into serous cavities; and

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[1] *Vide* paragraph relating to Hydatid of Pleura.

[2] Operations in which, to reach hydatids on the convex surface of the liver, it was necessary first to traverse the thorax.

[3] By this statement we mean that the deaths were due to some other intercurrent or coincident disease, unconnected with the hydatids, as proved by necropsy.

that, at best, it leaves the dead organism in place. In pulmonary hydatids there is a special risk of suffocative flooding.

2. Removal of the parasite by incision is an effectual and, with proper care, a reasonably safe proceeding; it should be the recognised and general practice.

3. No other treatment is justifiable in suppurating or ruptured hydatids, if we except those in which spontaneous evacuation by the natural channels is in progress and urgent symptoms absent.

4. Lindemann's operation, in which, after removal of the parasite, the cavity of the adventitious sac is left to drain externally, has stood the test of a large experience with favourable results, and is probably the best and safest procedure for general application. Possibly, however, Bond's operation, in which, after evacuation, the emptied adventitious sac is left behind, may prove to be more satisfactory in certain cases, the limits of which have yet to be determined by the test of experience.

Hydatids in the various Viscera of the Body

Distribution of hydatids in the body.—In 1000 autopsies performed in the mortuary of the Adelaide Hospital, South Australia, forty-nine bodies contained hydatids, that is, about 5 per cent. Eleven of these were cases of multiple hydatids; in five, two organs were infested; and in six, three or more of the viscera. In thirty-six instances the liver was involved; in nine the lungs; in six the spleen; in five the kidney; in five the peritoneum; in four the brain, and in one the heart. In a more extended table compiled by Thomas, comprising for all countries nearly 1900 cases, the frequency with which different organs are attacked is shown by the following percentages: liver, 57; lungs, 11·6; kidney, 4·7; brain, 4·4; spleen, 2·1; heart, 1·8. Peritoneum, omentum, and mesentery, 1·4.

Hydatid of the liver.—*Symptoms.*—Aching about the right shoulder may be felt, and, if the hydatid be large, a sense of weight and distension about the right hypochondrium. Actual pain is rare, but when suppuration supervenes it is often acute, and an excruciating hepatic colic attends the passage of membranes along the bile-ducts. The functions of the stomach and bowels are seldom interfered with, even when the cyst is so large as to fill and distend the abdomen. Not infrequently, at an autopsy, a parasite of no small size is discovered, which has occasioned no symptoms during life or none sufficient to attract attention.

Physical signs.—These will vary with the size and situation of the parasite; if it be small and deep-seated they will be absent. If on the upper surface, there may be bulging of the right side of the chest—at first only at the lower part, but later almost throughout with a more open curve to the costal arch, and widening and bulging of the intercostal spaces, even beyond the level of the ribs. The thoracic hepatic dulness is increased upwards, in one case it was as high as the first rib; it is often dome-shaped, in the front, the side, or the back of the chest. Percussion in the intercostal spaces gives the sensation of great resistance. The heart may be displaced to the left, or be pushed bodily forwards, so as to increase the force and area of the palpable impulse. If the parasite be large and in the substance of the liver, the size of the organ is manifestly increased, either generally or locally. The liver margin is depressed, even to the floor of the pelvis; its outline may be normal, descending at one point or with a more or less pedunculated outgrowth. The surface is uniformly smooth, or bulged at one spot, the bulging being either regularly convex or more or less lobulated; or, if the hydatid be multiple, the liver may be studded with prominent bosses like cancerous nodules. The enlargement is generally firm, and often elastic. The sense of fluctuation is very rarely elicited, percussion seldom yields the hydatid thrill. Jaundice in the absence of suppuration is very unusual, though it has been noted when membranes have entered and blocked the bile-ducts, or the cyst has pressed upon them in the portal fissure. Ascites is so uncommon as to be a pathological curiosity.

Hydatid of the liver often suppurates, either immediately after aspiratory puncture, tapping with trochar and canula, or accidental injury; sometimes this event occurs spontaneously, being due, occasionally at any rate, to rupture of a bile-duct into the cyst. The symptoms induced may be quite insignificant; but more often pyrexia of the remittent type supervenes with general constitutional disturbance, rigors and wasting; the tumour becomes painful and tender, increases noticeably in size, and the skin over it may grow red and resemble a pointing abscess. Jaundice is frequent.

Unless dealt with surgically a hydatid of the liver will extend, and discharge itself in one of several directions, as follows: (i.) Into the alimentary tract most commonly—either into the intestine or, if in the left lobe of the liver, into the stomach. The tumour may thus become tympanitic from entry of gas. The membranes, white or bile-stained, may be vomited or passed per anum; and this evacuation may persist for weeks or months, with eventual complete recovery or death from exhaustion. (ii.) Into a bronchial tube, after the formation of adhesions between the liver, diaphragm and lung, generally the right. Skins are expectorated, which are colourless, or in some cases deeply bile-stained. When all are thus removed the cavity contracts and health is restored. On the other hand, the patient often dies from exhaustion, the result of prolonged suppuration with hectic symptoms; or from profuse hæmoptysis, gangrene of the lung, or suffocation due to obstruction of the air-passages by a large piece of membrane or an unruptured daughter cyst. (iii.) Into the pleural sac, producing pleuritis generally suppurative, or pyo-pneumo-thorax from associated ulceration into a bronchus or the bowel. (iv.) Into the peritoneal cavity, setting up an intense and generally fatal peritonitis. (v.) Through the abdominal wall. (vi.) Into the biliary passages, inducing biliary colic with or without jaundice. (vii.) Into the pericardial sac. (viii.) Into the hepatic veins in the substance of the liver, whence the membranes are carried into the pulmonary arteries, and cause sudden death or rapidly fatal syncope.

Diagnosis.—Hydatid has to be distinguished—A, from other diseases of the liver causing enlargement; B, from extra-hepatic affections.

A 1. Lardaceous disease may be simulated by a parasite so deep in the substance of the liver as to cause no globular swelling on its surface, and big enough to enlarge the organ downwards. An associated enlargement of the spleen, and albuminuria, with a history of long-continued suppuration, would indicate waxy liver. When the amyloid condition is due to syphilis the organ may be nodulated from the contraction of fibroid trabeculæ, the result of obsolete gumma, and may thus simulate multiple superficial hydatids. Such syphilitic livers, however, are generally painful and tender, and are often immobile on deep inspiration, owing to adhesions from old perihepatitis. A history of syphilis, the existence of present or the evidence of past manifestations will assist in the diagnosis, until the exploring needle decide at once and finally.

A 2. Cancer of the liver may cause uniform enlargement, local bulging, or multiple bosses, and so resemble hydatids. Pain, tenderness and jaundice suggest cancer, provided suppuration can be excluded by the absence of pyrexia, rigors, and so forth. Cancerous cachexy and wasting may be manifest: on the other hand, the patient may be too young to render cancer probable.

A 3. Tropical abscess can only be confounded with a suppurating hydatid. The infrequency of hydatids in the tropics, and of tropical abscess in temperate zones, and the fact that tropical abscess of the liver is in the vast majority of cases preceded or accompanied by dysentery, will aid in forming a decision; though this is not of much moment, as the treatment of the two complaints is identical.

A 4. Nutmeg liver from morbus cordis. A hydatid may exist in the liver of a patient with heart disease, but a local bulging cannot be simple congestion. Aspiration will resolve the difficulty. A patient with heart disease may have had a hydatid removed from the right lobe of the liver, and a year or two later he may appear with a greatly enlarged left lobe, pyrexia, local tenderness, and some jaundice. The previous hydatid suggests a second parasite, now suppurating; but if careful inquiry reveal acute rheumatic pains at the onset of pyrexia, improvement on administration of salicylate of sodium, and gradual subsidence of the hepatic enlargement, the point will be decided; or if necessary an exploratory puncture may be made.

A 5. Cirrhosis of the liver during the hypertrophic stage may give rise to a general increase in its size. Sometimes a cirrhosis is partial, and occasions a local bulging of the viscus which may very closely resemble a hydatid tumour. In cirrhosis, however, we generally find a history of alcoholism and gastric disturbance; often also the aspect of over-stimulation: in cirrhosis, again, the liver-edge may be hard and its surface palpably granular.

A 6. A distended gall-bladder may exactly resemble a hydatid springing from the under surface of the liver, and projecting downwards from the lower margin. Both tumours may be somewhat movable, elastic, and obscurely fluctuating. The former is generally larger below and narrower above, and a hydatid the reverse, but not always. A history of sudden pain and then a gradual enlargement would suggest obstruction by a gall-stone; but such obstruction, with patency of the common duct and no jaundice, is of rare occurrence. Exploratory puncture will distinguish at once if the fluid be clear, watery, and free from albumin, or if any hooklets or membranes be withdrawn. But it must be remembered that colourless serum or bile-stained fluid may be found both in a gall-bladder and in a dead hydatid, or pus if they have suppurated.

A 7. Simple cysts of the liver are seldom large enough to be recognised during life. A concomitant nodulated enlargement of the spleen and of both kidneys would suggest cystic disease, though multiple hydatids might be present in all these organs. A needle would withdraw serum instead of the non-albuminous hydatid fluid.

B. Extra-hepatic affections.

B 1. Hydronephrosis. Usually, on deep inspiration, the fingers can be insinuated above a renal tumour, though sometimes a renal cyst is adherent to the liver, and continuous with its lower margin. Such a tumour fills the posterior lumbar region more than a hepatic hydatid, and the colon may be detected in front of it. The cyst may be lobulated; but a hydatid cyst also is sometimes obscurely lobulated. Should sudden diminution of the tumour occur, with coincident increase of the quantity of urine voided, it must be remembered that this event might happen also from the rupture of a hydatid into the pelvis of the kidney; in this case, however, it would probably be followed by the evacuation of pieces of membrane by the urethra. Aspiration might reveal urine more or less altered, albuminous fluid, pus, blood or colloid material; or, on the other hand, hooklets or membrane. Sometimes, however, the fluid withdrawn from a hydronephrosis is clear and limpid, with no albumin or but a trace, and much chloride of sodium, thus closely resembling hydatid fluid.

B 2. Effusion into the right pleural sac generally gives an area of dulness, whose upper limit slopes obliquely downwards and forwards from the spine; whereas in hydatid the upper margin of dulness often descends as it approaches the backbone. If the pleural effusion be loculated by old adhesions this test does not apply; nor if the patient has habitually leaned forwards during his illness, in which case the upper limit of pleural dulness may be higher in front. In pleural effusion a history may be obtained of acute pain and pyrexia at the onset. A friction sound does not aid in the diagnosis, as it may be present in either complaint.

B 3. Hydatid at the base of the right lung is usually indistinguishable from a parasite on the convexity of the liver. If, however, it be not situated at the extreme base the existence of a line of resonance between it and the normal hepatic dulness might render a diagnosis possible.

B 4. Ovarian tumour grows from below upwards, and generally an area of resonance intervenes between it and the liver: a hydatid grows from the liver downwards, and very rarely enters the pelvis.

B 5. Ascites can only be confounded with hydatid when the latter is so immense as to fill the whole abdomen, or when the former is of such nature as to prevent the intestines from floating forwards to the abdominal wall. Resonance in the flanks and iliac regions would indicate hydatids; an aspirator needle would settle the matter at once.

B 6. A phantom tumour would disappear on the administration of an anæsthetic.

Hydatid of the lung.—*Symptoms.*—Prior to rupture. If the cyst be small, no symptoms may be noticed; cough, however, is generally present, varying in severity, but rarely paroxysmal as in pertussis. Hæmoptysis, due to active congestion from irritation, to passive distension from pressure, or to a localised pneumonia, usually occurs sooner or later, either copiously or as mere streaks in the mucous sputum. Occasionally this symptom is absent throughout. A feeling of weight or discomfort, or the sensation of a foreign body in the chest, may be recorded, but these are uncommon. Dyspnœa increases with the volume of the cyst, but is sometimes slight, even when the tumour is very large; it is rarely paroxysmal, but it may be urgent, and due to pressure on the pulmonary artery or vein. There is no pyrexia unless pneumonia or pleurisy be excited, and only under these circumstances is there any wasting.

Physical signs may be wanting if the cyst be small and deeply seated; but when large there may be local swelling, which may be limited to a small area. It happens rarely that a rib is eroded from pressure, and that part of the cyst projects beyond the chest wall. Under such circumstances the disease may look very like an extra-thoracic fluid tumour; but its nature may be recognised by a diminution in size when the patient lies down. If very large, the intercostal spaces may be widened and somewhat prominent, and may communicate an elastic semifluctuant sensation on percussion. The area where the cyst comes to the surface is quite dull, and yields a marked sense of resistance. If a layer of lung intervene between the cyst and the chest wall a subtympanitic or even a Skodaic note may be elicited. The respiratory murmur may be weak or even abolished, as also the vocal resonance. The heart may be displaced to the right or to the left, according to the situation of the parasite; or be so pressed forwards as to give a greatly increased area of palpable cardiac pulsation. Rarely does œdema of one or both arms ensue from pressure on intra-thoracic veins.

When rupture takes place into a bronchus a violent suffocative cough arises, with expectoration of watery fluid, pieces of hydatid membrane and blood. This may be scanty, or may be so abundant as to threaten or even to terminate life; generally there is urgent dyspnœa. Also after rupture, cough, of varying frequency and violence, continues until all the cyst is expelled; exacerbations occur at irregular intervals, when much muco-pus may be raised, and many skins, fragments of the original cyst, and perhaps daughter cysts recently ruptured. The sputa may be fœtid, and hæmorrhage, which may be profuse or even fatal, may come on at any time, and be accounted for by supposed varices, degenerations, or aneurysms of the pulmonary vessels on the walls of the hydatid cavity. No deterioration of the general health may be apparent, although large quantities of membrane may have been coughed up during many months; on the other hand, pyrexia, wasting and hectic may supervene and rapidly exhaust the patient. Skins may be expectorated abundantly, and yet a careful examination of the chest will fail to reveal their source; as this may be a cavity deep in the substance of the lung which, contracting on its gradually diminishing contents, gives none of the classical signs of a vomica. Usually, however, the physical signs are those ordinarily found in a pulmonary cavity—for example, in phthisis—and vary as widely in different cases: at one time they may be ill defined, and then, after a profuse expectoration, well marked.

Hydatid of the pleura.—Very rarely a cyst has been found in the pleural cavity. It is probably impossible to diagnose a parasite so situated from one in the substance of the lung. Nor can its exact site be determined even when one or two ribs have been excised and the hydatid cavity laid open. For a pulmonary hydatid in its growth reaches the visceral pleura, which becomes fused with the thin adventitious capsule, and subsequently with the parietal layer; so that when incised no pleural cavity is opened, but the scalpel passes direct from the parietal pleura into the sac. In fact, it is almost certain that many hydatids supposed to be pleural are really pulmonary hydatids, which have become superficial.

Diagnosis.—1. From phthisis pulmonalis. When unruptured, hydatid disease resembles incipient phthisis in the short, dry cough, repeated hæmoptysis, and perhaps in some shortness of breath and abnormal physical signs at one spot in the chest; its hydatid nature is determined by the following considerations:—The signs are most often not at the apex; when they are, they are exceedingly rarely bilateral. The dulness is sharply defined, with weakened breath sound or respiratory silence, and an absence of moist râles. There is no pyrexia. The general health has undergone little or no deterioration, and although the symptoms may have existed for some months, the strength has not failed. The sputa will supply no tubercle bacilli, and a hypodermic needle will draw off hydatid fluid.

When ruptured it may be very difficult to distinguish a hydatid cavity from a phthisical vomica, unless it be situated in the base, as most frequently it is, the rest of the lung being healthy. Phthisical vomicæ, moreover, are very rare in children. If the disease is bilateral it is probably phthisical, for symmetrical pulmonary hydatids, though not unknown, are uncommon. Diarrhœa or laryngeal disease suggests phthisis; nevertheless the former may occur, as a hectic symptom, in prolonged and profuse suppuration from a pulmonary hydatid. The expectoration even of a microscopic fragment of hydatid membrane is conclusive. The membranes, however, frequently undergo gelatiniform degeneration, and may thus easily be overlooked by the physician; on the other hand, the patient may mistake shreds of tough, consistent mucus for pieces of "skins." Tubercle bacilli in the sputum prove the presence of phthisis, but they do not disprove that of hydatid, for now and then the two affections coexist.

Gangrene of the lung resembles hydatid in the presence of a cavity, and the voiding of fœtid sputa; but it generally runs a very acute course, and membranes are absent from the expectoration.

2. Pleural effusion is closely simulated by a hydatid at the base of the lung. Pain and pyrexia, or a recent history of them, will indicate the existence of the former. These symptoms may, however, occur in hydatid likewise, and may be caused by pleuritis due to irritation by the parasite. Dyspnœa is less marked in hydatid, owing to its slow growth and to the accommodation effected by bulging, etc. The line of dulness may help; in a hydatid it may be hemispherical above, in pleural effusion it generally slopes obliquely upwards from front to back. In a localised empyema the dulness might be dome-shaped, but in this case the pyrexia, pain and wasting might decide. Displacement of the heart to the right to an extent disproportionate to the area of dulness on the chest wall, indicating a much larger accumulation of fluid in the chest than is revealed by the superficial dulness, would suggest a hydatid of the left base.

Treatment of pulmonary hydatids.—When the hydatid is unruptured a portion of one or two ribs should be excised, the cyst laid open, the membranes removed, and the cavity efficiently drained. When there are bilateral hydatids, after one has been extirpated, sufficient time should be allowed for contraction of its cavity before the parasite on the other side is attacked. If there be two on the same side of the chest, and both have been recognised (though this discovery is very difficult), they may be dealt with in one operation, through separate incisions. The results are eminently satisfactory (*vide* table on p. 1132). Treatment by aspiration is inadmissible; for, as has been stated elsewhere in this section, there is a danger of death during the performance of this apparently simple operation. The bronchial tubes open directly and freely into the cavity in which the hydatid lies; and when by aspiration a certain quantity of its contained fluid has been removed, the cyst collapses, tears widely open, and the hydatid liquid rushes up the bronchi, down adjacent ones, and into those of the other side, thus causing a flooding of the lung which may be fatal. If the hydatid be already ruptured, and the cysts are being expectorated with little or no pus, with no pyrexia, and no failure in health, it is better to temporise; the patient will, most likely, cough up all the membranes, and a spontaneous cure will be effected. If, however, after rupture a cavity be recognisable, and there be profuse purulent or fœtid expectoration, with fever and constitutional disturbance, the proper course is to lay it freely open, remove the membrane, and drain efficiently. This condition may arise within three days of simple aspiration, and forms another objection to this procedure.

Hydatid of the spleen.—*Symptoms.*—One-half of the recorded cases were unsuspected during life and recognised after death, which would indicate that symptoms are frequently absent. Weight and pain may be felt, and great discomfort on bending forwards. The parasite may rupture into the left lung, into the bowel, or through the parietes of the body.

Physical signs.—A tumour, with the classical characters of a splenic enlargement, is present: smooth if the parasite be solitary; lobulated, if multiple; sometimes increasing upwards in the chest, sometimes downwards through the left side of the abdomen even into the pelvis, and yielding, in some cases, a perfect hydatid thrill.

Diagnosis.—1. A cyst in the left lobe of the liver is often quite indistinguishable from a hydatid of the spleen; occasionally isolation of the left edge of the liver and detection of the splenic notch will render a diagnosis possible.

2. *From lardaceous spleen.*—A circumscribed prominence favours a diagnosis of hydatid. On the other hand, uniform enlargement of the liver, a history of syphilitic disease, or prolonged suppuration with the coexistence of albuminuria, would contra-indicate its presence.

3. *From the enlarged spleen of hepatic cirrhosis.*—Here there are usually definite signs of the primary disease—slight jaundice, piles, melæna, hæmatemesis, or marked gastric derangement. Ascites comes on at a later stage.

4. *From abscess of the spleen.*—A diagnosis from suppurating hydatid is probably impossible, as the previous existence of the living parasite may easily have been overlooked by a patient.

Treatment.—The cyst should be opened and drained. The result is favourable. Death has, however, followed from hæmorrhage consequent upon sloughing of the adventitious capsule.

Hydatid of the kidney.—*Symptoms.*—Weight and distension, if large.

Physical signs.—A tumour in the lumbar region of the abdomen, to which an impulse is readily communicable from the loin; on deep inspiration, the fingers may be insinuated above it, isolating it from the liver and the spleen. It is smooth and uniform, if single; or lobulated, if multiple; more or less movable; with or without a hydatid thrill; separated from the liver by an area of resonance and with colon resonance—if this be present—in front of it.

Course.—It may exist for many years without affecting the general health, die, and become obsolescent or rupture into the pelvis of the kidney. The latter is the more common event. Pieces of membrane, daughter cysts, scolices, and, generally, a little blood are then passed by the urethra. This may be the first indication of the presence of the parasite, and if the cyst be small, no tumour may be discoverable in the loin. The passage of membranes may occasion attacks of renal colic so violent as to induce convulsions, or they may pass along the ureter without pain. Recovery not infrequently comes about, it may be after years of such discharges. The hydatid may suppurate and then burst into the pelvis and cause pyuria. So, too, it may ulcerate into the alimentary canal at some point, into the peritoneal cavity, or into the lung and discharge into a bronchus—in which case the prognosis is rather unfavourable—or even externally. When large, it may be so destructive as to prove fatal.

Diagnosis.—The determination of the renal origin of the cyst is fairly easy, especially on the left side. If, associated with a tumour in the kidney, we have a discharge by the urethra of hydatid products, the diagnosis is complete. Such discharge, however, without a renal tumour is not sufficient; for a hydatid of the pelvic pouch of the peritoneum is nearly as common, and this may open into the bladder. 1. The greatest difficulty is found in distinguishing between a hydatid and a hydronephrosis. In both a renal cyst is felt, in both it may be smooth, round, painless, movable, elastic, and with a perfect hydatid thrill. If it be lobulated it is more likely to be a hydronephrosis; but multiple hydatids or even a solitary one may be lobulated. If a hydatid tumour elsewhere should coexist, the probability of a renal parasite is much greater. If, however, there be a history of urinary trouble, such as the passing of calculi or of large quantities of urine with a corresponding subsidence of the tumour, a hydronephrosis would be the more likely. In these cases even the aspirator needle will not always decide. Of course if scolices or shreds of membrane be withdrawn, an absolute diagnosis is possible, but not otherwise; for though the aspiration of urine would favour hydronephrosis, yet this is said to pass by osmosis into hydatids, to the extent of forming deposits of triple phosphate crystals in the interior of daughter cysts, or even calculi as large as peas. Though clear limpid fluid, exactly resembling that of a hydatid, be evacuated, giving no albumin, or only a trace, and abundance of sodic chloride, it may, as likely as not, be a hydronephrosis, which not infrequently has similar contents. Even a trace of urea does not negative hydatid fluid, of which, in minute quantities, it is a normal constituent. The presence of albumin in large quantity, though common in hydronephrosis, may be found in a hydatid which has recently died. Sometimes, therefore, the distinction between the two renal affections is an impossibility. Fortunately the treatment demanded is the same for both, namely, free incision and drainage.

2. Cystic disease of the kidney, congenital or acquired, may closely

resemble multiple renal hydatids. Implication of both kidneys would suggest the former; and a palpable cyst in the liver with one kidney also involved, the latter.

3. *Ovarian and parovarian cysts.*—These grow from below upwards, and are generally known by their proper signs on combined vaginal and abdominal examination.

When suppurating, a hydatid cyst must be distinguished from pyelitis, simple or calculous; pyonephrosis; renal tuberculosis; and abscess, renal or perinephric. The special products of the hydatid, tubercle bacilli, or fragments of calculus discovered in the urine, are probably the only distinctions.

Hydatid of the omentum, mesentery, and peritoneum.—*Physical signs.*—One or more tumours are visible and palpable, generally very movable, both by the hands of the examiner and on change of position; they appear also to be unconnected directly with any of the abdominal viscera.

Diagnosis.—Their diagnosis from omental sarcomas in the young, and even from uterine myomas, and malignant disease in the pelvis, when they are multiple, is often impossible without puncture; and their nature is frequently determined only during an exploratory laparotomy.

They should be removed; to them Bond's method is particularly applicable.

Hydatid of the brain.—*Symptoms.*—An innocent slowly-growing intracranial tumour, giving rise to symptoms varying with its site and size. Headache nearly always occurs, generally early in the case, and may persist throughout. Its character varies; thus it may be severe and constant, paroxysmal, or aggravated by movements of the head; in some cases the pain is general, in others referred to the neighbourhood of the parasite, felt down the back of the neck, or as a trigeminal neuralgia. Vertigo and vomiting are common. Vision is frequently affected. Partial or total blindness may arise, in one or both eyes; most often gradually, at times suddenly. A cyst anywhere may cause it. Optic neuritis and atrophy are infrequent, but may be marked, especially if a meningitis be excited. Epileptiform convulsions are often noted, and occasionally clonic spasms limited to one side of the face, or to one-half of the body. Rarely they may be tonic. Distinct aphasia has been produced. Ataxy on standing, staggering gait, and motor paralysis, either paraplegic, hemiplegic, or facial, may be found—though all these may be absent, even if a cerebral hemisphere be occupied by quite a large cyst.

Diagnosis.—The diagnosis involves three points—the existence of a tumour, its site, and its nature. The first two must be decided on ordinary principles of cerebral diagnosis: a hydatid presents no special features. An opinion as to its nature may be formed from the following considerations:—1. In countries infested by this parasite its possibility should never be forgotten. 2. It may cause a uniform enlargement of the skull; or, in children, either a distinct local bulging, or a thinning, so as to yield egg-shell crackling, or even a perforation. 3. The mean age of patients with tubercular tumour is 12½ years, that of echinococcus is 22 years; therefore a cerebral tumour in a child is more likely to be tubercular than hydatid, in a young adult the reverse may be expected. Cerebral hydatids are about fourteen times as common as cerebellar; therefore a cerebellar tumour is probably not a hydatid. Tubercular tumour is as common in the cerebellum as in the cerebrum; therefore a cerebellar tumour in a child is much more likely to be tubercular than hydatid. 4. A hydatid elsewhere in the patient would strongly confirm the diagnosis of a cerebral hydatid. 5. It has been proposed to pierce the skull with an instrument like a watchmaker's drill, and explore with a large hypodermic needle. Membrane or hooklets might be withdrawn; but the composition of hydatid fluid so exactly resembles the cerebro-spinal that, without these, it would be impossible with certainty to distinguish the one from the other.

Prognosis.—Some cases after spontaneous perforation of the skull and discharge, either spontaneous or after simple incision of the skull, have terminated in recovery, but such cases are rare. Most patients died, either suddenly during an epileptiform fit, while vomiting, or more or less rapidly from coma, or from various intercurrent complaints. The duration will depend on the situation and rapidity of growth. Life has continued apparently for five years after the first symptoms were noted.

Treatment.—But one course is open, to trephine and remove the parasite—a procedure which has been successfully carried out.

Hydatid of the spinal cord is very rare. The cyst may be wholly within the spinal canal, or partly within and partly outside. In some cases it invades it from the tissues or cavities adjacent; in others it originates within the canal, and extends by atrophy of bone, or through the intervertebral foramina, into the muscular tissues of the back, or into the thoracic and abdominal cavities in front. The *symptoms* are those of compression of the cord with perhaps a supervening myelitis. The nature of the disease might be suspected if a hydatid were found in some other part of the body, but a diagnosis could only be made, with certainty, if part of the parasite projected externally, as has actually happened; in which case its nature could be determined by aspiration. Hitherto all cases have proved fatal; but, if detected, the cyst should be incised, and removed.

Hydatid of the heart.—This is found very rarely, and only as a pathological curiosity. It has never been diagnosed during life, and is not known to have given rise to any symptoms.

Extra-visceral hydatids.—These fall within the province of the surgeon rather than of the physician, and need not be specially discussed in this place. The same general principles of treatment, however, are applicable to these, and with less risk; but when a long bone becomes the nidus of the parasite, amputation of the affected member may be necessary.

J. C. Verco.
E. C. Stirling.

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J. C. V.
E. C. S.

ADDENDA

SERO-DIAGNOSIS OF TYPHOID FEVER

(WIDAL'S TEST)

See p. 791, Vol. I.

THIS method was first described by Dr. Fernand Widal of Paris, on the 26th of June 1896.[1] It is based on the action which the blood of patients affected with typhoid fever has on cultures of the Eberth's bacillus.

Widal has recommended two kinds of methods of applying his test.

I. **The slow methods,** which may also be described as *macroscopical.*

(*a*) Take a tube of sterilised neutral bouillon. Add to the bouillon a small quantity of the blood or blood serum to be tested (the quantity of serum should be about $\frac{1}{10}$ part of the whole amount of fluid). Inoculate this mixture of serum and bouillon with typhoid bacilli. Incubate this tube at a temperature of 37° C. for about 20 hours.

If the blood be that of a typhoid patient, the culture medium will at the end of this time be clear, or nearly so; and the bacilli that have grown will form at the bottom of the test-tube a sediment of clumps composed of agglomerated bacilli. *If the blood, on the contrary, has been taken from a normal person, or from one affected with a disease other than typhoid fever,* the fluid will be turbid, and there will be hardly any sediment at the bottom of the tube.

(*β*) It is not necessary to mix the bouillon and serum before sowing the bacilli; if the serum of a typhoid patient be added to a young culture of the typhoid bacillus in bouillon, an abundant precipitation of agglomerated bacilli will produce, in less than two or three hours, a distinct sediment composed of small clumps. This way of applying the test is, however, not usually so clear as the one described above.

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[1] Dr. Grünbaum, who was working with Professor Max Gruber in Vienna at the beginning of 1896, very nearly anticipated Widal; he reports in his papers published in the *Lancet* for 19th Sept. and 19th Dec. 1896, a series of cases, some of which were observed as far back as March 1896. It even appears that a paper had been sent by him to one of the English periodicals not more than a month after Widal's first communication. Grünbaum's investigation had for its object to ascertain whether there were any relation between the degree of immunisation and the agglutinating properties of the blood. It is to be regretted that he should not have published some of his results sooner. By the end of July Widal had already published his methods in full, and a large number of observations. The methods Grünbaum recommends, if properly carried out, are simple and effective.

II. **The quick or microscopical method.**—This method very closely resembles the second naked-eye test just described.

Take a drop of blood or of the serum to be examined. Dilute with 9 parts of neutral bouillon. Mix on a slide or cover-glass a drop of this $\frac{1}{10}$ dilution of the serum with one or more drops of a young (24-hours-old) culture of the typhoid bacillus.

Instead of a culture in bouillon, an emulsion of the bacillus can be prepared by taking a small quantity of a 24-hours-old culture on agar, or of a culture on gelatine, and rubbing this thoroughly in a small quantity of bouillon or normal saline solution.

Cover the mixed drops with a cover-glass, or, if the mixture has been made on a cover-glass, place this cover (film downwards) on a slide.

Examine the preparation at once with the microscope. (The most convenient powers to use are such as will magnify from 200 to 300 times in diameter; but the reaction can be seen with a very low power, and when it is well marked, even with the naked eye.)

If the serum, or blood, be that of a typhoid patient in the 2nd, 3rd, 4th, or 5th week of the illness, the reaction will in most cases appear almost instantaneously. Within one or two minutes the bacilli, instead of moving rapidly as when they are in presence of non-typhoid blood, become sluggish and, in many cases, motionless. They run together as if moved by some force of attraction, and form clumps of various sizes. This *agglomeration phenomenon* may sometimes be so complete that after a space of time, varying between 5 minutes and 20 minutes, hardly any bacilli remain free between the clumps. In a few instances the reaction is not distinct before the end of the first or second hour; but these cases are exceptional.

In a certain proportion of cases, after an interval of from a few to 24 or 48 hours, the bacilli become granular. Usually, however, if kept under favourable conditions, the bacilli retain their normal appearance, and even continue to grow and multiply; in such cases the bacilli generally form long filaments.

In the case of healthy or of diseased persons not affected with typhoid fever, no such reaction is obtained. It is true that when too large a proportion of blood is used even the serum of healthy persons may give rise to agglomeration of the bacilli. But the phenomenon in such cases is far less clear and well defined than in cases of typhoid fever, and generally comes on very slowly. Grünbaum is of opinion that to avoid this source of fallacy a dilution of the blood serum greater than that recommended by Widal is necessary.

In my experience imperfect agglomeration has been very seldom a source of difficulty. A careful observer, controlling his observations at every point, should be able to avoid any fallacy from this source.

It is unnecessary to give here complete statistical data of the results already obtained by that method. By putting together the cases published by Widal, Widal and Sicard, Chantemesse, Achard, Courmont, Grünbaum, Delépine, Delépine and Sidebotham, Wyatt Johnston, Hausalter, Stern, and others, it is already possible to obtain a list of more than 200 cases of typhoid fever in which the reaction above described has been obtained. In a larger number still of persons not affected with typhoid fever the reaction has been sought for and not obtained. Thoelen and Mills, and Durham have failed to obtain constant results by this method, but their failures are not in accordance with the experience of others.

In enteric fever the reaction has been obtained by Widal on the 4th and 5th days; and some American observers have reported the reaction at an earlier date still. It must be remembered, however, that during the first week the reaction is often slow and not quite clear, and that to establish a clear diagnosis re-examination is very often necessary. During the five weeks following the first, the agglomeration phenomenon can generally be obtained rapidly and clearly; in some cases, indeed, the reaction has been observed for months after an attack of typhoid fever, but we cannot yet say how long the blood of a typhoid patient retains its specific action on the typhoid bacillus. In eight persons who had recovered from typhoid fever for more than one year, Widal observed the reaction in one only. It is certain that the reaction gradually diminishes in intensity; and that, after a few years, it disappears entirely (that is, when the experimental conditions given above are observed).

It is unnecessary to discuss here the probable nature of the substance causing the reaction, to which the name of agglutinin has been given by Gruber; but as the formation of clumps does not seem to be the result of an agglutination, it will be better for the present to avoid the use of this term. The word *agglomeration* indicates quite clearly what is seen, and is preferable for general use.

Various modifications of Widal's methods have been used in practice with the view of rendering the method more easily applicable in practice. Thus Wyatt Johnson has adopted the plan, suggested by Widal himself, of drying the blood for sending it to a distance.

From the first, that is immediately after Widal's first publication, I found it advantageous to collect the blood in sealed pipettes, and to make the various dilutions of serum, and the mixture of serum and culture, on the slide or cover-glass by means of a platinum loop of definite size, adapted to take up small drops of constant weight as ascertained by careful and repeated weighings.

This method of measuring fluids by means of the platinum loop has been much used in bacteriology, and R. Pfeiffer has shown more than once that it can be used for work of great accuracy. Dr. Sidebotham and myself have satisfied ourselves by independent observations of the trustworthiness of measurements obtained by this method.

The platinum loop has many advantages over the graduated pipettes recommended by other observers; it is easily and rapidly sterilised, and enables us to measure very small quantities of fluid—a matter of importance when we have to deal with single drops of blood.

Widal, and Widal and Sicard have shown that drying and even partial putrefaction will not prevent the blood from giving this reaction, though a certain loss of power is observed; they also found that *blister fluid* had the same properties on the blood serum.

Milk and tears of typhoid patients have also been found to behave in the same way, though they are less active than the blood serum. Urine cannot be used, as the results it yields are generally ambiguous.

The *heating* of the blood or milk to a temperature of 60° to 75° C. causes a loss of agglomerating power; at 80° C. this power is entirely lost.

This method may be said to be a most happy application of a number of scientific discoveries which had been made between the year 1889 and the date of Widal's announcement of his results.

The first to observe and clearly to describe the agglomeration phenomenon, for which such an important application has been found, were Charrin and Roger (1889). These authors describe very clearly the appearance presented by culture of the Bacillus pyocyaneus in the blood serum of animals immunised against this bacillus. The only thing they do not seem to have noticed is the rapidity of the immobilisation and clumping of the bacilli on mixing the bacilli with the serum. They did not use diluted serum; but, as they made control experiments with the serum of unvaccinated animals, their observations cannot be dismissed as of no value. In 1891 Metschnikoff observed the same thing with regard to the Vibrio Metschnikovi; and he went so far as to suggest that the phenomenon was probably of general importance.

R. Pfeiffer, since 1894, has made numerous experiments to show that when a micro-organism is introduced into the peritoneal cavity of a guinea-pig strongly immunised against that particular microbe, a degeneration of the microbe follows, which, under definite conditions, is fatal to it. This phenomenon, which Pfeiffer attributes chiefly to the action of the serum, is a specific one. It is undoubtedly closely connected with the phenomenon utilised by Widal, yet it was incapable of the same applications; and Pfeiffer has again and again expressed the belief that his phenomenon could only be observed in presence of living tissues. Metschnikoff and Bordet showed that it was not necessary to introduce the bacteria into the peritoneal cavity of a living animal; but that peritoneal fluid, and the blood serum of immunised animals even outside the body, in test-tubes or in the hanging drop, had a strong action on the bacteria against which the animals had been protected.

Bordet, in 1895, gave quite a clear description of the effects which the serum has on the microbes, outside the body, and mentioned specially their immobilisation and agglomeration.

This subject was then taken up by Max Gruber, with whom, later, Durham went to study. These two authors carefully studied the conditions necessary to make the clumping reaction available for the diagnosis of pathogenetic organisms. It remained for Widal to discover that the action of the serum was one observed *not only when immunity had been well established, but soon after infection had occurred.* Moreover, it occurred to Widal *that, if the serum could be used for the diagnosis of the bacillus, the reverse must be true.* So that instead of taking the serum of an animal artificially immunised against the typhoid bacillus to test whether a microbe were the typhoid bacillus indeed, he took a definite typhoid bacillus of undoubted origin, and used it to test whether the serum of a doubtful case of typhoid fever were capable of acting upon this bacillus. The older methods necessitated the previous isolation and cultivation of the typhoid bacillus, a process which, in practice so far, has proved remarkably fruitless for purposes of diagnosis. This new method does away with the difficulty, and generally permits an accurate diagnosis to be made in a few minutes. Such a discovery must be looked upon as one of the most remarkable practical applications of the science of bacteriology to the practice of medicine.

Sheridan Delépine.

P.S.—In the *Lancet* for 6th March 1897, Professor Wright and Surgeon-Major Smith have shown that the above method is applicable both to the differential diagnosis between Malta fever and typhoid fever, and to the direct diagnosis of Malta fever itself. Thus also the specific quality of the Micrococcus melitensis (Bruce) is more strongly established, and the identity of certain other unclassed fevers—as, for instance, in the North-West of India—with the Malta fever is verified.

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S. D.

SUPPLEMENT TO THE ARTICLE "PLAGUE"

See p. 917, Vol. I.

In the epidemics which have prevailed since this article was written, the importance of certain points there insisted upon, namely, the existence of the plague virus in the soil, as shown, among other facts, by the infection of rats, and the occurrence of a milder form of plague, or *pestis minor*, has been strongly confirmed. There are, however, some new facts and occurrences which require a short notice. These relate to—(i.) geographical distribution and extension; (ii.) therapeutics; (iii.) the laws of quarantine.

Geographical Distribution.—Since the great epidemic of plague of 1894 in Canton and Hong-Kong, the disease recurred in 1896, but was far less destructive in Hong-Kong. The mortality in Canton is not accurately known. An extension has also taken place northward to Amoy, to the island of Formosa, and perhaps to other places. A more alarming appearance is that of plague in Bombay, where it has prevailed with considerable severity from the autumn of 1896 (probably about September) till the present time (March 1897). The origin of the Bombay epidemic is attributed to infected persons or things from Hong-Kong; but the importation was not clearly traced. From Bombay it has spread to Poonah and other parts of the Bombay Presidency, probably through direct conveyance by infected persons.

A very destructive epidemic of plague has also prevailed at Karachi, plausibly attributed to importation from Bombay. Calcutta has been threatened, but the cases reported are few and doubtful. It should be remembered that, though there have been some previous epidemics in tropical or semi-tropical parts of India, such as Rajputana and Cutch, the disease has never become endemic there. The mean annual temperature of these regions is far above that of those parts of Southern China which lie in the same latitude; and there seems reason to hope that the disease, though favoured by the winter temperature, may not survive the heat of an Indian summer, and may even not become endemic. This does not, of course, apply to Northern India, where the plague is clearly endemic, though narrowly limited in distribution. It is also known that two cases of plague were brought to London in the autumn of 1896, and satisfactorily isolated in the Seamen's Hospital, so that no spread of the disease took place.

Therapeutics.—The system of serum therapeutics for plague referred to on p. 936 has now been practically tested in a very promising way. M. Yersin thus describes his researches and experience on this subject. In 1894 it had been established that a serum could be obtained from horses by inoculation of plague-bacilli, which was *preventive* if inoculated into mice of 20 grammes weight, in a dose of $\frac{1}{10}$ c.c.; so that if inoculated with plague-bacilli twelve hours later they proved to be immune. It was also *curative*, in doses of 1 to 1·5 c.c., if injected twelve hours after inoculation with plague.

The preparation of serum from horses was continued at the Pasteur Institute of Paris; and early in 1896 Yersin established a laboratory at Nha Trang, in Annam, for the same purpose. With serum from this institution, and also with a supply obtained from the Pasteur Institute, Yersin went to Canton to find cases of plague, but was able to treat one case only, in a very early stage. In this case the symptoms were completely removed in about twelve hours by two injections of 10 c.c., and perfect recovery followed. Two other cases were afterwards treated with equal success with serum which Yersin left behind him. Following out the same plan at Amoy, he treated twenty-three cases, of which twenty-one recovered. Six patients in whom treatment was begun on the first day of the disease, recovered in from twelve to twenty-four hours with from 20 to 40 c.c. serum. Six patients treated on the second day recovered in three or four days after injection of 30 to 50 c.c. In four cases treated on the third day recovery was slower, but the cure was complete with doses of 40-60 c.c. Three patients treated on the fourth day were cured in five to six days with doses of 20 to 50 c.c. Of four patients taken at the fifth day, two recovered with doses of 60-90 c.c., while two who were already in a desperate condition succumbed. Thus out of twenty-six cases, including persons of both sexes and all ages, twenty-four recovered.

Experience has shown that the treatment is more efficacious the earlier the stage of the disease. When treatment is begun in the first two days of the attack, fever and all alarming symptoms disappear with astonishing rapidity, buboes go away under the eye without suppuration. In cases treated at a later stage larger doses are required, and suppuration of the buboes is not always prevented; but it does not last long. Convalescence is comparatively rapid. When the disease is far advanced, the heart being weak and the pulse and respiration irregular, the serum is powerless.

There are no inconveniences attending the treatment beyond occasional transitory pain from the injection; and no important accident has resulted from the use of the serum.

It is noteworthy that though the serum was sent from Paris to Annam, and thence carried to China and Amoy, its efficacy was not impaired by keeping or transit in a hot climate.

These results are of the highest interest and importance, and, if confirmed by larger experience, seem to promise a reduction in the mortality from plague beyond all anticipation.[1]

Laws of Quarantine. — Since my article was written, the old quarantine law, administered by the Privy Council (p. 937), has been formally abolished in this country, and all preventive regulations are subject to the action of the Local Government Board.

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[1] *Annales de l'Institut Pasteur*, 1897, vol. xi. p. 81.

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An important communication respecting the Plague in Hong-Kong in 1894 was made to the Epidemiological Society of London by Mr. James Cantlie, which is fully reported in the *Lancet*, 2nd and 9th January 1897. A paper by Dr. Lowson appeared in the same journal subsequently.

J. F. P.

ADDENDUM TO "YELLOW FEVER"

See p. 385, *ante*.

SINCE the article on Yellow Fever passed into the hands of the printer, an important announcement has been made of the discovery by Dr. Giuseppe Sanarelli of the bacillus of this disease. Similar announcements have so frequently been made, exciting hopes which further investigations have disappointed, that, until the particulars are published and the experiments verified, a certain amount of scepticism is not only justifiable but obligatory. Those, however, who are in a position to know something of Sanarelli's researches and results are unanimous in the conviction that the microbe of Yellow Fever has at last been discovered. We are thus encouraged to look forward with considerable confidence to the forthcoming account of his researches, which I had hoped might have appeared in time to be included in this addendum.

Sanarelli has been occupying himself in the preparation of a protective or curative serum. In this direction, we are told, his experiments have been very extensive—more than 2000 animals, including rabbits, goats, sheep, monkeys and horses, having been vaccinated. If he succeeds in this aim, the treatment recommended in this work may be largely modified, and the reader is advised to bear this in mind.

The discovery of the microbe of Yellow Fever may also be expected to throw a new light on some obscure points in the etiology, not of this disease only, but also of allied affections.

A. D.

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